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(54) Title: PROTEIN COMPLEXES OF CELLULAR NETWORKS UNDERLYING THE DEVELOPMENT OF CANCER AND OTHER DISEASES

(57) Abstract: The present invention relates to protein complexes involved in cellular processes which have been shown to be critical for the development of various forms of cancer, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.



PROTEIN COMPLEXES OF CELLULAR NETWORKS UNDERLYING THE DEVELOPMENT OF CANCER AND OTHER DISEASES

1. FIELD OF THE INVENTION

The present invention relates to protein complexes involved in cellular processes which have been shown to be critical for the development of various forms of cancer, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

2. BACKGROUND OF THE INVENTION

Despite enormous efforts, cancer still remains as one of the major types of diseases affecting humans. Although significant progress has been made in the development of therapies, the situation in the cancer field in general, an urgent need for new therapies, i.e. new medicaments exists. To progress, a better understanding of the molecular mechanisms is necessary, serving as a basis for a directed identification of suitable drug targets. To further address the biological context of proteins which have been identified to be key players in the development of several cancers, protein interactors were searched for. By applying a novel approach, it was shown that the proteins, rather then interacting with individual proteins, form aggregations which could also be described as "protein complexes". The proteins which have been analysed as being key players in processes underlying the development of cancer are further described below.

<u>Pot1</u>

In all eukaryotic species the ends of chromosomes have specialized non-coding DNA squences that, together with associated proteins, are known as telomers. Telomeres act as protective caps, preventing both degradation of the ends of chromosomes and their recognition as double-strand breaks, which otherwise would result in aberrant recombination. Telomeric DNA consists of simple tandem repeats of guanine-rich sequences (hexanucleotide repeats d(TTAGGG) in vertebrates). The extreme 3' end is

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single stranded and typically 100-200 bases long. It is extensively associated with a variety of proteins. One of them is the Pot1 protein (protection of telomeres) which was described in fission yeast and humans.

However, despite various lines of evidence were presented so far, the full biological context of Pot1 and thus, the role of the proteins associated with Pot1 in the cell and particularly in pathogenic conditions have remained largely elusive.

Her2

Growth factors and their transmembrane receptor tyrosine kinases play important roles in cell proliferation, survival, migration and differentiation. One group of growth factors, comprising epidermal growth factor (EGF)-like proteins and neuregulins, stimulates cells to divide by activating members of the EGF receptor (EGFR) family, which consists of the EGFR itself and the receptors known as HER2-4. Her receptors exist as monomers but dimerize on ligand binding. No Her2-specific ligand has been identified but Her2 is the preferred heterodimerization partner for other Her receptors. Amplification of the Her2 gene or overexpression of the Her2 protein is associated with malignancy and a poor prognosis in breast cancer.

Thus, despite various lines of evidence were presented so far, the full biological context of Her2 and thus, the role of the proteins associated with Her2 in the cell and particularly in pathogenic conditions have remained largely elusive.

Ringo1

Cyclin-dependent kinases (Cdks) are essential regulators of the eukaryotic cell division cycle. Cdks are subject to many modes and levels of regulation in response to both intracellular and extracellular signals. They are activated through their association with regulatory subunits called cyclins that are synthesized and degraded in a cell cycle-dependent manner. CDK-cyclin complexes are in turn regulated by the cyclin-dependent kinase inhibitors (CDKIs), which generally inhibit cell cycle progression. Recently it has been shown that Cdk1 (Cdc2) and Cdk2 can also be activated by a protein called Ringo. Ringo has no similarity to cyclins at the amino acid sequence level. Cdk-Ringo complexes may be active under conditions in which cyclin-bound Cdks are inhibited and therefore play different regulatory roles.

Thus, despite various lines of evidence were presented so far, the full biological context of Ringo and thus, the role of the proteins associated with Ringo in the cell and particularly in pathogenic conditions have remained largely elusive.

Gab1

The GAB1 complex plays an important role in various cytokines, growth factors, and antigen receptors signaling. Several signaling molecules, such as MET (HGFR), EGFR, SHP2, PI 3-kinase, GRB2, SHIP2, SHC, SOS, PLC gamma, and CRK, have been found associated directly or indirectly with GAB1. GAB1 is expressed in all tissues examined except liver, lung, and kidney. The larger splice variant was cloned and used in this experiment as a entry point of retrieval. We have seen, that complex formation is mediated via tyrosine phosphorylation of GAB1 (data available in a separate document). Upon induction of tyrosine phosphorylation with vanadate as well as HGF, we have identified most of the known interactor, validating our findings, as well as several novel components that include, detailed below that may influence GAB1 activity and play important roles in proliferation and metastatic signaling. We have also identified several novel interactors in the absence of tyrosine phosphorylation that could be sequestered by GAB1 to keep them inactive.

However, despite various lines of evidence were presented so far, the full biological context of Gab1 and thus, the role of the proteins associated with Gab1 in the cell and particularly in pathogenic conditions have remained largely elusive.

Bcl2

Bcl-2 family proteins are key regulators of programmed cell death. The Bcl-2 family includes both anti- and pro-apoptotic proteins with opposing biological functions in either inhibiting or promoting cell death. High expression of anti-apoptotic members such as Bcl-2 and Bcl-XL commonly found in human cancers contributes to neoplastic cell expansion and interferes with the therapeutic action of many chemotherapeutic drugs. The functional blockade of Bcl-2 or Bcl-XL could either restore the apoptotic process in tumor cells or sensitize these tumors for chemo- and radiotherapies.

Thus, despite various lines of evidence were presented so far, the full biological context of Bcl-2 and thus, the role of the proteins associated with Bcl-2 in the cell and particularly in pathogenic conditions have remained largely elusive.

3. SUMMARY OF THE INVENTION

An object of the present invention was to identify protein complexes formed around protein which have been shown to be critical for the development of various forms of cancer, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of these proteins and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
(a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
(b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins,

wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under lowstringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM

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Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the provisio that the complex comprises at least one protein selected from table 1, fifth column of a given complex.
- 5. The complex of any of No. 1 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in at least one biochemical activity as stated in table 3.

- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps: expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of a protein complex obtainable by a process according to any of No. 9 11.
- 13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

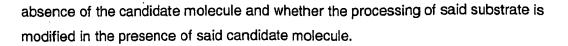
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
- (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
- 16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
- 18. A kit comprising in one or more containers:
 - (a) the complex of any of No. 1 8 and/or the proteins of No. 13 and/or
 - (b) an antibody according to No. 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of No. 1 8 and/or a protein of No. 13 and/or
 - (d) cells expressing the complex of any of No. 1 8 and/or a protein of No. 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
- The kit according to No. 18 for processing a substrate of a complex of any one of No.
 1 8.

- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 21. Array, preferably a microarray, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for modifying a substrate of a complex of any one of No. 1 8 comprising the step of bringing into contact a complex of any of No. 1 8 with said substrate, such that said substrate is modified.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or a protein according to No. 13.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 25. A method for screening for a molecule that binds to a complex of any one of No. 1 8 and/or a protein of No. 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene

dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.

- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.

- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the



- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
- 41. The complex of any one of No. 1 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of No. 1 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

3.1 **DEFINITIONS**

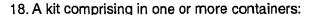
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The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or anorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator $1\mu g \text{ mi}^{-1}$, $10\mu g$ ml⁻¹, $100\mu g$ ml⁻¹, $500\mu g$ ml⁻¹, 1mg ml⁻¹, 10mg ml⁻¹ or 100mg ml⁻¹. Any combination of the above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats



- (a) the complex of any of No. 1 8 and/or the proteins of No. 13 and/or
- (b) an antibody according to No. 17 and/or
- (c) a nucleic acid encoding a protein of the complex of any of No. 1-8 and/or a protein of No. 13 and/or
- (d) cells expressing the complex of any of No. 1 8 and/or a protein of No. 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.
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- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or a protein according to No. 13.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 25. A method for screening for a molecule that binds to a complex of any one of No. 1 8 and/or a protein of No. 13, comprising the following steps:

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- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

- 30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said

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amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
- 41. The complex of any one of No. 1 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.

- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of No. 1 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as D. melanogaster, C. elegans or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

TABLES:

Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

Table 4: Medical Applications of the Complexes of the invention

First column ('Name of complex'): Lists the name of the protein compelxes as used herein

Second column ('Medical application'): lists disorder, diseases, disease areas etc. which are treatable and/or preventable and/or diagnosable etc. by therapeutics and methods interacting with/acting via the complex.

4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The protein complexes of the present invention and their component proteins are described in the Tables 1 - 4. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, infra, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by

reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ ID NO 1 - 198), and can be obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of 32P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO4, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be used are well known in the art. Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μ g/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably forms a complex that binds to an anti-complex antibody. Such an antibody is further described infra.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include in vitro recombinant DNA and synthetic techniques and in vivo recombinant techniques (genetic recombination). Expression of nucleic acid sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be

selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of β -galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.

Once recombinant component protein molecules are identified and the complexes or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses

such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent molecules. Due to the degeneracy of nucleotide coding sequences, other DNA sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those

containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative, homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated in vitro or in vivo, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further in vitro modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and in vitro site-directed mutagenesis (Hutchinson et al., 1978, J. Biol. Chem. 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, Nature 310:105-111).

reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred

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Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization, by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open

EBV-hybridoma technique (Cole et al., 1985, Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally Current Protocols in Immunology 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al., 1991, Bio/Technology 9:1370-1372; Hay et al., 1992, Hum. Antibod. Hybridomas 3:81-85; Huse et al., 1989, Science 246:1275-1281; Griffiths et al., 1993, EMBO J. 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be

polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, Nature 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, Immunol. Today 4:72), the

produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, Science 240:1041-1043; Liu et al., 1987, Proc. Natl. Acad. Sci. USA 84:3439-3443; Liu et al., 1987, J. Immunol. 139:3521-3526; Sun et al., 1987, Proc. Natl. Acad. Sci. USA 84:214-218; Nishimura et al., 1987, Canc. Res. 47:999-1005; Wood et al., 1985, Nature 314:446-449; and Shaw et al., 1988, J. Natl. Cancer Inst. 80:1553-1559); Morrison, 1985, Science 229:1202-1207; Oi et al., 1986, Bio/Techniques 4:214; U.S. Patent 5,225,539; Jones et al., 1986, Nature 321:552-525; Verhoeyan et al., 1988, Science 239:1534; and Beidler et al., 1988, J. Immunol. 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, Int. Rev. Immunol. 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, Bio/technology 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')2 fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')2 fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

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In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see infra), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

4.3 DIAGNOSTIC, PROGNOSTIC, AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are those as listed in table 4

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

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Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof, comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein.

Such diseases and disorders include, but are not limited to neurodegenerative disease such as listed in table 4.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to

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determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of

the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell, 1996, Microbiol. Rev. 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, Clin. Obstet. Gynecol 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, Clin. Biochem. 29:5-9). Such isolations can be used as methods of diagnosis, described, supra.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an abberant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein

complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example those listed in table 4.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, Science 244:1288-1292. In one embodiment, a therapeutic is

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1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectfully, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, infra.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in diseases or disorders where an in vitro (or in vivo) assay (see infra) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).

A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, Gene Therapy 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, infra. Ribozyme therapy involves the administration, induced expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, Annals of Medicine 28:499-510; Gibson, 1996, Cancer and Metastasis Reviews 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, Gene Therapy 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, infra.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of an component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using in vitro assays or animal models, examples of which are described, infra.

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In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, infra) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by electrophoresis sulfate polyacrylamide gel (SDS-PAGE), sodium dodecvl immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing component mRNA concurrently or separately using, e.g., Northern assays, dot blot

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

analysis, in situ hybridization, etc.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject. In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, Clinical Pharmacy 12:488-505; Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; Morgan and Anderson, 1993, Ann. Rev. Biochem. 62:191-217; and May, 1993, TIBTECH 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, Current Protocols in Molecular Biology, John Wiley & Sons, NY; and Kriegler, 1990, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being

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inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid is directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et

al., 1993, Meth. Enzymol. 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, Biotherapy 6:291-302, which describes the use of a retroviral vector to deliver the mdr1 gene to hematopoetic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, J. Clin. Invest. 93:644-651; Kiem et al., 1994, Blood 83:1467-1473; Salmons and Gunzberg, 1993, Human Gene Therapy 4:129-141; and Grossman and Wilson, 1993, Curr. Opin. in Genetics and Devel. 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, Curr. Opin. Genet. Devel. 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, Human Gene Therapy 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, Science 252:431-434; Rosenfeld et al., 1992, Cell 68:143-155; and Mastrangeli et al., 1993, J. Clin. Invest. 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, Proc. Soc. Exp. Biol. Med. 204:289-300.

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene from these that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation,

microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, Meth. Enzymol. 217:599-618; Cohen et al., 1993, Meth. Enzymol. 217:618-644; Cline, 1985, Pharmac. Ther. 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoetic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoetic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoetic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut,

embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, Cell 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, Meth. Cell Biol. 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown in tissue culture (Rheinwald, 1980, Meth. Cell Bio. 2A:229; Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoetic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance in vitro of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, J. Clin. Invest. 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, J. Cell Physiol. 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, Proc. Natl. Acad. Sci. USA 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, supra.

4.4.2 USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX FORMATION OR PROTEIN COMPLEX/PROTEIN ACTIVITY

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described supra.

The antisense nucleic acids of the invention can be oligonucleotides that are double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting the expression of component protein nucleic acid sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded

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or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. USA 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. USA 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, BioTechniques 6:958-976), or intercalating agents (see, e.g., Zon, 1988, Pharm. Res. 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, xanthine, 4-acetylcytosine, hypoxanthine, 5-chlorouracil, 5-iodouracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-(carboxyhydroxylmethyl)uracil, 5-carboxymethylaminomethyluracil, dihydrouracil, β-D-galactosylqueosine, inosine, 1-methylguanine, 2.2-dimethylquanine. 1-methylinosine. N6-isopentenviadenine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, 7-methylguanine, β-D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracii-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2-a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual B-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially avail-able from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligo-nucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced in vivo such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto

et al., 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. USA 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or in situ hybridization), or by observing the ability of RNA from the cell type to be translated in vitro into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, in situ hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, infra), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to

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determine the antisense cytotoxicity in vitro, and then in useful animal model systems. prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex activity or formation, e.g., anti- complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" gel diffusion precipitin reactions, immunoradiometric assays. immunoassavs. immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2nd Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 infra, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.

One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component

proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

4.6 <u>SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS</u> OF THE INVENTION

1.

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependend on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation. Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an abberant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening for a molecule that binds a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art in vitro, in vivo or ex vivo. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such

contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fifth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, infra, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out in vitro, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, infra.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, Adv. Exp. Med. Biol. 251:215-218; Scott and Smith, 1990, Science 249:386-390; Fowlkes et al., 1992, BioTechniques 13:422-427; Oldenburg et al., 1992, Proc. Natl. Acad. Sci. USA 89:5393-5397; Yu et al., 1994, Cell 76:933-945; Staudt et al., 1988, Science 241:577-580; Bock et al., 1992, Nature 355:564-566; Tuerk et al., 1992, Proc. Natl. Acad. Sci. USA 89:6988-6992; Ellington et al., 1992, Nature 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, Science 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, Gene 73:305-318; Fowlkes et al., 1992, BioTechniques 13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of

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complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g., 125 I or 3 H), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or β -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g., ³H-leucine or ³⁵S-methionine, radiolabeling by post-translational iodination with ¹²⁵I or ¹³¹I using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with ³²P using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotinacetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described infra, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of

incubation is typically at least 15 seconds, but longer times are preferred to allow binding equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., Proteins, Structures, and Molecular Principles, 2nd Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, Proc. Natl. Acad. Sci. USA 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin, β-casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrolidine, nonionic detergents (NP40, Triton X-100, Tween 20, Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed

extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, supra.

In another specific embodiments screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, J. Pharm. Biomed. Anal. 7:155-168; Mitchell et al. 2002, Nature Biotechnol. 20:225-229; Petricoin et al., 2002, Lancet 359:572-577; Templin et al., 2001, Trends Biotechnol. 20:160-166; Wilson and Nock, 2001, Curr. Opin. Chem. Biol. 6:81-85; Lee et al., 2002 Science 295:1702-1705; MacBeath and Schreiber, 2000, Science 289:1760; Blawas and Reichert, 1998, Biomaterials 19:595; Kane et al., 1999, Biomaterials 20:2363; Chen et al., 1997, Science 276:1425; Vaugham et al., 1996, Nature Biotechnol. 14:309-314; Mahler et al., 1997, Immunotechnology 3:31-43; Roberts et al., 1999, Curr. Opin. Chem. Biol. 3:268-273; Nord et al., 1997, Nature Biotechnol. 15:772-777; Nord et al., 2001, Eur. J. Biochem. 268:4269-4277; Brody and Gold, 2000, Rev. Mol. Biotechnol. 74:5-13; Karlstroem and Nygren, 2001, Anal. Biochem. 295:22-30; Nelson et al., 2000, Electrophoresis 21:1155-1163; Honore et al., 2001, Expert Rev. Mol. Diagn. 3:265-274; Albala, 2001, Expert Rev. Mol. Diagn. 2:145-152, Figeys and Pinto, 2001, Electrophoresis 2:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, Nature Biotechnol. 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH2 or N-oxy-succinamate.

The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use

of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturating protein gel.

If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

Alternatively, members of the protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnel, 2001, Curr. Opin. Chem. Biol. 5:572-577; Lee, 2001, Trends Biotechnol. 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, Ann. Clin. Biochem. 37:119-

145; Vely et al., 2000, Methods Mol. Biol. 121:313-321; Slepak, 2000, J. Mol Recognit. 13:20-26.

Exemplary assays useful for measuring the Bcl-2 binding activity of the Bcl2-complex include but are not limited to those described in Hanada M et al., 1995, J Biol Chem, 270:11962-9.

Exemplary assays useful for measuring the cytochrome c release activity from mitochondria of the Bcl2-complex include but are not limited to those described in Bossy-Wetzel E and ., 2000, Methods Enzymol, 322:235-42.

Exemplary assays useful for measuring the apoptosis induction activity of the Bcl2-complex include but are not limited to those described in Bossy-Wetzel E and ., 2000, Methods Enzymol, 322:15-8.

Exemplary assays useful for measuring the Cell motility acitvity of the Gab1 signalling complex include but are not limited to those described in Petrelli Annalisa et al., 2002, Nature, 416:187-90.

Exemplary assays useful for measuring the Focus forming activity of the Gab1 signalling complex include but are not limited to those described in Giordano S et al., 1997, Proc Natl Acad Sci U S A, 94:13868-72.

Exemplary assays useful for measuring the Tumorigenicity and experimental metastatic activity of the Gab1 signalling complex include but are not limited to those described in Giordano S et al., 1997, Proc Natl Acad Sci U S A, 94:13868-72.

Exemplary assays useful for measuring the In vitro invasion activity of the Gab1 signalling complex include but are not limited to those described in Giordano S et al., 1997, Proc Natl Acad Sci U S A, 94:13868-72.

Exemplary assays useful for measuring the Soft agar colony formation activity of the Gab1 signalling complex include but are not limited to those described in Giordano S et al., 1997, Proc Natl Acad Sci U S A, 94:13868-72.

Exemplary assays useful for measuring the Scatter activity of the Gab1 signalling complex include but are not limited to those described in Ponzetto C et al., 1996, J Biol Chem, 271:14119-23.

Exemplary assays useful for measuring the kinase activity of the Her2 complex include but are not limited to those described in Engelman J A et al., 1998, J Biol Chem, 273:20448-55.

Exemplary assays useful for measuring the diacylglycerol kinase activity of the Her2 complex include but are not limited to those described in Walsh J P et al., 1992, Methods Enzymol, 209:153-62.

Exemplary assays useful for measuring the sphingosine kinase activity of the Her2 complex include but are not limited to those described in Olivera A et al., 2000, Methods Enzymol, 311:215-23.

Exemplary assays useful for measuring the kinase activation of the Ringo 1 complex include but are not limited to those described in Karaiskou A et al., 2001, J Biol Chem, 276:36028-34.

Exemplary assays useful for measuring the DNA binding activity of the telomere capping complex include but are not limited to those described in Baumann P et al., 2001, Science, 292:1171-5.

Exemplary assays useful for measuring the TRF2 binding activity of the telomere capping complex include but are not limited to those described in Song K et al., 2000, FEBS Lett, 481:81-5.

Exemplary assays useful for measuring the RAP1 binding activity of the telomere capping complex include but are not limited to those described in Li B et al., 2000, Cell, 101:471-83.

4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided to a cell expressing the complex machinery, or, in the case of candidate proteins, can be provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, supra.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein component composition of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant, e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the

interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries, recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, Nature 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, Nature 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single, random sequence of amino acid residues; Medynski, 1994, Bio/Technology 12:709-710, which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, J. Med. Chem. 37:1233-1251. Simply by way of other examples, a combinatorial library may be prepared for use, according to the methods of Ohlmeyer et al., 1993, Proc. Natl. Acad. Sci. USA 90:10922-10926; Erb et al., 1994, Proc. Natl. Acad. Sci. USA 91:11422-11426; Houghten et al., 1992, Biotechniques 13:412; Jayawickreme et al., 1994, Proc. Natl. Acad. Sci. USA 91:1614-1618; or Salmon et al., 1993, Proc. Natl. Acad. Sci. USA 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, Proc. Natl. Acad. Sci. USA 89:5381-5383 describe "encoded combinatorial chemical libraries." that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, Proc. Natl. Acad. Sci. USA 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, crosslink by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, Proc. Natl. Acad. Sci. USA 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side chains attached not to the α carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids, -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid; -Abu, -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, β-alanine, designer amino acids such as β-methyl amino acids, C-methyl amino acids, N-methyl amino acids,

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GAMMA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,

- (xliv) "SIMILAR TO OROSOMUCOID 1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO OROSOMUCOID 1" encoded by a nucleic acid that hybridizes to the "SIMILAR TO OROSOMUCOID 1" nucleic acid or its complement under low stringency conditions,
- (xIv) "SMC5 PROTEIN" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMC5 PROTEIN" encoded by a nucleic acid that hybridizes to the "SMC5 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xIvi) "SQUAMOUS CELL CARCINOMA ANTIGEN 1" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SQUAMOUS CELL CARCINOMA ANTIGEN 1" encoded by a nucleic acid that hybridizes to the "SQUAMOUS CELL CARCINOMA ANTIGEN 1" nucleic acid or its complement under low stringency conditions,
- (xlvii) "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" encoded by a nucleic acid that hybridizes to the "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (xlviii) "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" encoded by a nucleic acid that hybridizes to the "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" nucleic acid or its complement under low stringency conditions,
- (xlix) "Similar to diacylglycerol kinase delta" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to diacylglycerol kinase delta" encoded by a nucleic acid that hybridizes to the "Similar to diacylglycerol kinase delta" nucleic acid or its complement under low stringency conditions,
- (I) "TELOMERASE-BINDING PROTEIN P23" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "TELOMERASE-BINDING PROTEIN P23" encoded by a nucleic acid that hybridizes to the "TELOMERASE-BINDING PROTEIN P23" nucleic acid or its complement under low stringency conditions,

- (li) "TELOMERIC REPEAT BINDING FACTOR 2" (SEQ ID No.51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERIC REPEAT BINDING FACTOR 2" encoded by a nucleic acid that hybridizes to the "TELOMERIC REPEAT BINDING FACTOR 2" nucleic acid or its complement under low stringency conditions,
- (lii) "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" encoded by a nucleic acid that hybridizes to the "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" nucleic acid or its complement under low stringency conditions,
- (liii) "TRF1" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF1" encoded by a nucleic acid that hybridizes to the "TRF1" nucleic acid or its complement under low stringency conditions,
- (liv) "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" encoded by a nucleic acid that hybridizes to the "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (Iv) "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" encoded by a nucleic acid that hybridizes to the "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (Ivi) "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200



KDA HELICASE (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(Ivii) "WD-REPEAT PROTEIN AN11 HOMOLOG" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "WD-REPEAT PROTEIN AN11 HOMOLOG" encoded by a nucleic acid that hybridizes to the "WD-REPEAT PROTEIN AN11 HOMOLOG" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "38 KDA FK-506 BINDING PROTEIN HOMOLOG" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "38 KDA FK-506 BINDING PROTEIN HOMOLOG" encoded by a nucleic acid that hybridizes to the "38 KDA FK-506 BINDING PROTEIN HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (ii) "ANTIGEN NY-CO-7" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ANTIGEN NY-CO-7" encoded by a nucleic acid that hybridizes to the "ANTIGEN NY-CO-7" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" encoded by a nucleic acid that hybridizes to the "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" nucleic acid or its complement under low stringency conditions,
- (iv) "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (v) "BAF180" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAF180" encoded by a nucleic acid that hybridizes to the "BAF180" nucleic acid or its complement under low stringency conditions,
- (vi) "CASEIN KINASE II, ALPHA CHAIN" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "CASEIN KINASE II, ALPHA CHAIN" encoded by a nucleic acid that hybridizes to the "CASEIN KINASE II, ALPHA CHAIN" nucleic acid or its complement under low stringency conditions,

- (vii) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (viii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (ix) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,
- (x) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions,
- (xii) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,

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(xiii) "CENP-F KINETOCHORE PROTEIN" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENP-F KINETOCHORE PROTEIN" encoded by a nucleic acid that hybridizes to the "CENP-F KINETOCHORE PROTEIN" nucleic acid or its complement under low stringency conditions,

- (xiv) "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" encoded by a nucleic acid that hybridizes to the "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" nucleic acid or its complement under low stringency conditions,
- (xv) "DNA MISMATCH REPAIR PROTEIN MSH6" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA MISMATCH REPAIR PROTEIN MSH6" encoded by a nucleic acid that hybridizes to the "DNA MISMATCH REPAIR PROTEIN MSH6" nucleic acid or its complement under low stringency conditions,
- (xvi) "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xvii) "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" encoded by a nucleic acid that hybridizes to the "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELONGATION FACTOR 2 KINASE" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELONGATION FACTOR 2 KINASE" encoded by a nucleic acid that hybridizes to the "ELONGATION FACTOR 2 KINASE" nucleic acid or its complement under low stringency conditions,
- (xix) "FK506-BINDING PROTEIN 4" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

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"FK506-BINDING PROTEIN 4" encoded by a nucleic acid that hybridizes to the "FK506-BINDING PROTEIN 4" nucleic acid or its complement under low stringency conditions, (xx) "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" encoded by a nucleic acid that hybridizes to the "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" nucleic acid or its complement under low stringency conditions,

(xxi) "HDCMD34P" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDCMD34P" encoded by a nucleic acid that hybridizes to the "HDCMD34P" nucleic acid or its complement under low stringency conditions,

(xxii) "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" encoded by a nucleic acid that hybridizes to the "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" nucleic acid or its complement under low stringency conditions,

(xxiii) "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" encoded by a nucleic acid that hybridizes to the "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" nucleic acid or its complement under low stringency conditions,

(xxiv) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029" encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions,

(xxv) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxvi) "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)"

encoded by a nucleic acid that hybridizes to the "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxix) "MEPRIN A BETA-SUBUNIT PRECURSOR" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEPRIN A BETA-SUBUNIT PRECURSOR" encoded by a nucleic acid that hybridizes to the "MEPRIN A BETA-SUBUNIT PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxx) "MUTS" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MUTS" encoded by a nucleic acid that hybridizes to the "MUTS" nucleic acid or its complement under low stringency conditions,

(xxxi) "MYELOID LEUKEMIA FACTOR 2" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MYELOID LEUKEMIA FACTOR 2" encoded by a nucleic acid that hybridizes to the "MYELOID LEUKEMIA FACTOR 2" nucleic acid or its complement under low stringency conditions,

(xxxii) "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" encoded by a nucleic acid that hybridizes to the "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" nucleic acid or its complement under low stringency conditions,

(xxxiii) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC"

encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions,

(xxxiv) "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" encoded by a nucleic acid that hybridizes to the "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" nucleic acid or its complement under low stringency conditions,

(xxxv) "PROGRAMED CELL DEATH PROTEIN 2" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROGRAMED CELL DEATH PROTEIN 2" encoded by a nucleic acid that hybridizes to the "PROGRAMED CELL DEATH PROTEIN 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PROLIFERATING CELL NUCLEAR ANTIGEN" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROLIFERATING CELL NUCLEAR ANTIGEN" encoded by a nucleic acid that hybridizes to the "PROLIFERATING CELL NUCLEAR ANTIGEN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PROTEASOME SUBUNIT BETA TYPE 3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROTEASOME SUBUNIT BETA TYPE 3" encoded by a nucleic acid that hybridizes to the "PROTEASOME SUBUNIT BETA TYPE 3" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Pot1" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pot1" encoded by a nucleic acid that hybridizes to the "Pot1" nucleic acid or its complement under low stringency conditions.

(xxxix) "RAD50 HOMOLOGUE HSRAD50" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50 HOMOLOGUE HSRAD50" encoded by a nucleic acid that hybridizes to the "RAD50 HOMOLOGUE HSRAD50" nucleic acid or its complement under low stringency conditions,

(xl) "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" encoded by a nucleic acid that hybridizes to the "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" nucleic acid or its complement under low stringency conditions,

- (xli) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xlii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xliii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xliv) "SIMILAR TO OROSOMUCOID 1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO OROSOMUCOID 1" encoded by a nucleic acid that hybridizes to the "SIMILAR TO OROSOMUCOID 1" nucleic acid or its complement under low stringency conditions.
- (xlv) "SMC5 PROTEIN" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMC5 PROTEIN" encoded by a nucleic acid that hybridizes to the "SMC5 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xlvi) "SQUAMOUS CELL CARCINOMA ANTIGEN 1" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SQUAMOUS CELL CARCINOMA ANTIGEN 1" encoded by a nucleic acid that hybridizes to the "SQUAMOUS CELL CARCINOMA ANTIGEN 1" nucleic acid or its complement under low stringency conditions,

(xlvii) "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" encoded by a nucleic acid that hybridizes to the "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" nucleic acid or its complement under low stringency conditions,

(xlviii) "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" encoded by a nucleic acid that hybridizes to the "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" nucleic acid or its complement under low stringency conditions,

- (xlix) "Similar to diacylglycerol kinase delta" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to diacylglycerol kinase delta" encoded by a nucleic acid that hybridizes to the "Similar to diacylglycerol kinase delta" nucleic acid or its complement under low stringency conditions,
- (i) "TELOMERASE-BINDING PROTEIN P23" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERASE-BINDING PROTEIN P23" encoded by a nucleic acid that hybridizes to the "TELOMERASE-BINDING PROTEIN P23" nucleic acid or its complement under low stringency conditions.
- (Ii) "TELOMERIC REPEAT BINDING FACTOR 2" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERIC REPEAT BINDING FACTOR 2" encoded by a nucleic acid that hybridizes to the "TELOMERIC REPEAT BINDING FACTOR 2" nucleic acid or its complement under low stringency conditions,
- (lii) "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2"

encoded by a nucleic acid that hybridizes to the "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" nucleic acid or its complement under low stringency conditions, (Iiii) "TRF1" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF1" encoded by a nucleic acid that hybridizes to the "TRF1" nucleic acid or its complement under low stringency conditions,

- (liv) "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" encoded by a nucleic acid that hybridizes to the "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (Iv) "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" encoded by a nucleic acid that hybridizes to the "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (Ivi) "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (Ivii) "WD-REPEAT PROTEIN AN11 HOMOLOG" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "WD-REPEAT PROTEIN AN11 HOMOLOG" encoded by a nucleic acid that hybridizes to the "WD-REPEAT PROTEIN AN11 HOMOLOG" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (III) and comprising the following proteins:
- (i) "38 KDA FK-506 BINDING PROTEIN HOMOLOG" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "38 KDA FK-506 BINDING PROTEIN HOMOLOG" encoded by a nucleic

acid that hybridizes to the "38 KDA FK-506 BINDING PROTEIN HOMOLOG" nucleic acid or its complement under low stringency conditions,

- (ii) "ANTIGEN NY-CO-7" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ANTIGEN NY-CO-7" encoded by a nucleic acid that hybridizes to the "ANTIGEN NY-CO-7" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" encoded by a nucleic acid that hybridizes to the "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" nucleic acid or its complement under low stringency conditions,
- (iv) "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (v) "CASEIN KINASE II, ALPHA CHAIN" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASEIN KINASE II, ALPHA CHAIN" encoded by a nucleic acid that hybridizes to the "CASEIN KINASE II, ALPHA CHAIN" nucleic acid or its complement under low stringency conditions.
- (vi) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (vii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (viii) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,

- (ix) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions,
- (x) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,
- (xi) "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" encoded by a nucleic acid that hybridizes to the "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" nucleic acid or its complement under low stringency conditions,
- (xii) "DNA MISMATCH REPAIR PROTEIN MSH6" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA MISMATCH REPAIR PROTEIN MSH6" encoded by a nucleic acid that hybridizes to the "DNA MISMATCH REPAIR PROTEIN MSH6" nucleic acid or its complement under low stringency conditions,
- (xiii) "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xiv) "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" encoded by a nucleic acid that hybridizes to the "DNA-DIRECTED RNA

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POLYMERASE II 23 KDA POLYPEPTIDE" nucleic acid or its complement under low stringency conditions,

- (xv) "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" encoded by a nucleic acid that hybridizes to the "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" nucleic acid or its complement under low stringency conditions,
- (xvi) "HDCMD34P" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDCMD34P" encoded by a nucleic acid that hybridizes to the "HDCMD34P" nucleic acid or its complement under low stringency conditions,
- (xvii) "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" encoded by a nucleic acid that hybridizes to the "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" nucleic acid or its complement under low stringency conditions.
- (xviii) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xix) "MUTS" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MUTS" encoded by a nucleic acid that hybridizes to the "MUTS" nucleic acid or its complement under low stringency conditions,
- (xx) "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" encoded by a nucleic acid that hybridizes to the "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" nucleic acid or its complement under low stringency conditions,
- (xxi) "PROGRAMED CELL DEATH PROTEIN 2" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROGRAMED CELL DEATH PROTEIN 2" encoded by a nucleic acid that

hybridizes to the "PROGRAMED CELL DEATH PROTEIN 2" nucleic acid or its complement under low stringency conditions,

(xxii) "Pot1" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pot1" encoded by a nucleic acid that hybridizes to the "Pot1" nucleic acid or its complement under low stringency conditions,

(xxiii) "RAD50 HOMOLOGUE HSRAD50" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50 HOMOLOGUE HSRAD50" encoded by a nucleic acid that hybridizes to the "RAD50 HOMOLOGUE HSRAD50" nucleic acid or its complement under low stringency conditions,

(xxiv) "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" encoded by a nucleic acid that hybridizes to the "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" nucleic acid or its complement under low stringency conditions,

(xxv) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxvi) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxvii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" encoded by a nucleic

acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "SQUAMOUS CELL CARCINOMA ANTIGEN 1" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SQUAMOUS CELL CARCINOMA ANTIGEN 1" encoded by a nucleic acid that hybridizes to the "SQUAMOUS CELL CARCINOMA ANTIGEN 1" nucleic acid or its complement under low stringency conditions,

(xxix) "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" encoded by a nucleic acid that hybridizes to the "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" nucleic acid or its complement under low stringency conditions,

(xxx) "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" encoded by a nucleic acid that hybridizes to the "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" nucleic acid or its complement under low stringency conditions,

(xxxi) "TELOMERASE-BINDING PROTEIN P23" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERASE-BINDING PROTEIN P23" encoded by a nucleic acid that hybridizes to the "TELOMERASE-BINDING PROTEIN P23" nucleic acid or its complement under low stringency conditions,

(xxxii) "TELOMERIC REPEAT BINDING FACTOR 2" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERIC REPEAT BINDING FACTOR 2" encoded by a nucleic acid that hybridizes to the "TELOMERIC REPEAT BINDING FACTOR 2" nucleic acid or its complement under low stringency conditions,

(xxxiii) "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" encoded by a nucleic acid that hybridizes to the "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "TRF1" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF1" encoded by a nucleic acid that hybridizes to the "TRF1" nucleic acid or its complement under low stringency conditions,

(xxxv) "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" encoded by a nucleic acid that hybridizes to the "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxxvi) "WD-REPEAT PROTEIN AN11 HOMOLOG" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "WD-REPEAT PROTEIN AN11 HOMOLOG" encoded by a nucleic acid that hybridizes to the "WD-REPEAT PROTEIN AN11 HOMOLOG" nucleic acid or its complement under low stringency conditions,

- 4. The protein complex according to No. 1 comprising all but 1 55 of the following proteins:
- (i) "38 KDA FK-506 BINDING PROTEIN HOMOLOG" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "38 KDA FK-506 BINDING PROTEIN HOMOLOG" encoded by a nucleic acid that hybridizes to the "38 KDA FK-506 BINDING PROTEIN HOMOLOG" nucleic acid or its complement under low stringency conditions,
- (ii) "ANTIGEN NY-CO-7" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ANTIGEN NY-CO-7" encoded by a nucleic acid that hybridizes to the "ANTIGEN NY-CO-7" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" encoded by a nucleic acid that hybridizes to the "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" nucleic acid or its complement under low stringency conditions,
- (iv) "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions,

- (v) "BAF180" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAF180" encoded by a nucleic acid that hybridizes to the "BAF180" nucleic acid or its complement under low stringency conditions,
- (vi) "CASEIN KINASE II, ALPHA CHAIN" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASEIN KINASE II, ALPHA CHAIN" encoded by a nucleic acid that hybridizes to the "CASEIN KINASE II, ALPHA CHAIN" nucleic acid or its complement under low stringency conditions,
- (vii) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (viii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (ix) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,
- (x) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xi) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions,
- (xii) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,
- (xiii) "CENP-F KINETOCHORE PROTEIN" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENP-F KINETOCHORE PROTEIN" encoded by a nucleic acid that hybridizes to the "CENP-F KINETOCHORE PROTEIN" nucleic acid or its complement under low stringency conditions,
- (xiv) "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" encoded by a nucleic acid that hybridizes to the "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" nucleic acid or its complement under low stringency conditions,
- (xv) "DNA MISMATCH REPAIR PROTEIN MSH6" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA MISMATCH REPAIR PROTEIN MSH6" encoded by a nucleic acid that hybridizes to the "DNA MISMATCH REPAIR PROTEIN MSH6" nucleic acid or its complement under low stringency conditions,
- (xvi) "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xvii) "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DIRECTED RNA POLYMERASE II 23 KDA

POLYPEPTIDE" encoded by a nucleic acid that hybridizes to the "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" nucleic acid or its complement under low stringency conditions,

- (xviii) "ELONGATION FACTOR 2 KINASE" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELONGATION FACTOR 2 KINASE" encoded by a nucleic acid that hybridizes to the "ELONGATION FACTOR 2 KINASE" nucleic acid or its complement under low stringency conditions,
- (xix) "FK506-BINDING PROTEIN 4" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FK506-BINDING PROTEIN 4" encoded by a nucleic acid that hybridizes to the "FK506-BINDING PROTEIN 4" nucleic acid or its complement under low stringency conditions,
- (xx) "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" encoded by a nucleic acid that hybridizes to the "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" nucleic acid or its complement under low stringency conditions,
- (xxi) "HDCMD34P" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDCMD34P" encoded by a nucleic acid that hybridizes to the "HDCMD34P" nucleic acid or its complement under low stringency conditions,
- (xxii) "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" encoded by a nucleic acid that hybridizes to the "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" nucleic acid or its complement under low stringency conditions,
- (xxiii) "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" encoded by a nucleic acid that hybridizes to the "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" nucleic acid or its complement under low stringency conditions,
- (xxiv) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029"

encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions,

(xxv) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxvi) "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxvii) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxviii) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxix) "MEPRIN A BETA-SUBUNIT PRECURSOR" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEPRIN A BETA-SUBUNIT PRECURSOR" encoded by a nucleic acid that hybridizes to the "MEPRIN A BETA-SUBUNIT PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxx) "MUTS" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MUTS" encoded by a nucleic acid that hybridizes to the "MUTS" nucleic acid or its complement under low stringency conditions,

(xxxi) "MYELOID LEUKEMIA FACTOR 2" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MYELOID LEUKEMIA FACTOR 2" encoded by a nucleic acid that hybridizes

to the "MYELOID LEUKEMIA FACTOR 2" nucleic acid or its complement under low stringency conditions,

(xxxii) "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" encoded by a nucleic acid that hybridizes to the "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" nucleic acid or its complement under low stringency conditions,

(xxxiii) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC" encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions,

(xxxiv) "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" encoded by a nucleic acid that hybridizes to the "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" nucleic acid or its complement under low stringency conditions,

(xxxv) "PROGRAMED CELL DEATH PROTEIN 2" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROGRAMED CELL DEATH PROTEIN 2" encoded by a nucleic acid that hybridizes to the "PROGRAMED CELL DEATH PROTEIN 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PROLIFERATING CELL NUCLEAR ANTIGEN" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROLIFERATING CELL NUCLEAR ANTIGEN" encoded by a nucleic acid that hybridizes to the "PROLIFERATING CELL NUCLEAR ANTIGEN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PROTEASOME SUBUNIT BETA TYPE 3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROTEASOME SUBUNIT BETA TYPE 3" encoded by a nucleic acid that hybridizes to the "PROTEASOME SUBUNIT BETA TYPE 3" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Pot1" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pot1" encoded by a nucleic acid that hybridizes to the "Pot1" nucleic acid or its complement under low stringency conditions,

(xxxix) "RAD50 HOMOLOGUE HSRAD50" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50 HOMOLOGUE HSRAD50" encoded by a nucleic acid that hybridizes to the "RAD50 HOMOLOGUE HSRAD50" nucleic acid or its complement under low stringency conditions,

- (xI) "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" encoded by a nucleic acid that hybridizes to the "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" nucleic acid or its complement under low stringency conditions,
- (xli) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xlii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,
- (xliii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-

GAMMA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions,

(xliv) "SIMILAR TO OROSOMUCOID 1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO OROSOMUCOID 1" encoded by a nucleic acid that hybridizes to the "SIMILAR TO OROSOMUCOID 1" nucleic acid or its complement under low stringency conditions,

(xlv) "SMC5 PROTEIN" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMC5 PROTEIN" encoded by a nucleic acid that hybridizes to the "SMC5 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xlvi) "SQUAMOUS CELL CARCINOMA ANTIGEN 1" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SQUAMOUS CELL CARCINOMA ANTIGEN 1" encoded by a nucleic acid that hybridizes to the "SQUAMOUS CELL CARCINOMA ANTIGEN 1" nucleic acid or its complement under low stringency conditions,

(xlvii) "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" encoded by a nucleic acid that hybridizes to the "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" nucleic acid or its complement under low stringency conditions,

(xlviii) "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" encoded by a nucleic acid that hybridizes to the "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" nucleic acid or its complement under low stringency conditions,

(xlix) "Similar to diacylglycerol kinase delta" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to diacylglycerol kinase delta" encoded by a nucleic acid that hybridizes to the "Similar to diacylglycerol kinase delta" nucleic acid or its complement under low stringency conditions,

(I) "TELOMERASE-BINDING PROTEIN P23" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "TELOMERASE-BINDING PROTEIN P23" encoded by a nucleic acid that hybridizes to the "TELOMERASE-BINDING PROTEIN P23" nucleic acid or its complement under low stringency conditions,

- (li) "TELOMERIC REPEAT BINDING FACTOR 2" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERIC REPEAT BINDING FACTOR 2" encoded by a nucleic acid that hybridizes to the "TELOMERIC REPEAT BINDING FACTOR 2" nucleic acid or its complement under low stringency conditions,
- (lii) "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" encoded by a nucleic acid that hybridizes to the "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" nucleic acid or its complement under low stringency conditions,
- (Iiii) "TRF1" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF1" encoded by a nucleic acid that hybridizes to the "TRF1" nucleic acid or its complement under low stringency conditions,
- (liv) "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" encoded by a nucleic acid that hybridizes to the "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (iv) "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" encoded by a nucleic acid that hybridizes to the "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" nucleic acid or its complement under low stringency conditions,
- (Ivi) "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200

KDA HELICASE (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (Ivii) "WD-REPEAT PROTEIN AN11 HOMOLOG" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "WD-REPEAT PROTEIN AN11 HOMOLOG" encoded by a nucleic acid that hybridizes to the "WD-REPEAT PROTEIN AN11 HOMOLOG" nucleic acid or its complement under low stringency conditions.
- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the DNA binding activity, TRF2 binding activity or RAP1 binding activity.
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the telomere capping complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the telomere capping complex selected from
- (i) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (ii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (iii) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,
- (iv) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (v) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions,

- (vi) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,
- (vii) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029" encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and
- (xi) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC" encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

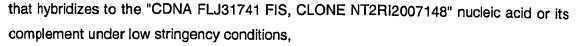
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.

- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as cancer such as solid tumours such as breast cancer, prostate cancer, lung cancer, colon cancer; cancer such as haematological cancers such as leukemia.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (ii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (iii) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,
- (iv) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS,

CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (v) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions,
- (vi) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,
- (vii) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029" encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC" encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as cancer such as solid tumours such as breast cancer, prostate cancer, lung cancer, colon cancer; cancer such as haematological cancers such as leukemia.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions,
- (ii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions,
- (iii) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions,
- (iv) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (v) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid



- (vi) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions,
- (vii) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029" encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC" encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of(a) exposing said complex, or a cell or organism containing telomere capping complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "38 KDA FK-506 BINDING PROTEIN HOMOLOG" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "38 KDA FK-506 BINDING PROTEIN HOMOLOG" encoded by a nucleic

acid that hybridizes to the "38 KDA FK-506 BINDING PROTEIN HOMOLOG" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "ANTIGEN NY-CO-7" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ANTIGEN NY-CO-7" encoded by a nucleic acid that hybridizes to the "ANTIGEN NY-CO-7" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" encoded by a nucleic acid that hybridizes to the "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BAF180" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAF180" encoded by a nucleic acid that hybridizes to the "BAF180" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "CASEIN KINASE II, ALPHA CHAIN" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASEIN KINASE II, ALPHA CHAIN" encoded by a nucleic acid that hybridizes to the "CASEIN KINASE II, ALPHA CHAIN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions, and/or

- (ix) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions, and/or
- (x) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "CENP-F KINETOCHORE PROTEIN" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENP-F KINETOCHORE PROTEIN" encoded by a nucleic acid that hybridizes to the "CENP-F KINETOCHORE PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" encoded by a nucleic acid that hybridizes to the "CHROMATIN ASSEMBLY FACTOR 1 SUBUNIT C" nucleic acid or its complement under low stringency conditions, and/or

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- (xv) "DNA MISMATCH REPAIR PROTEIN MSH6" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA MISMATCH REPAIR PROTEIN MSH6" encoded by a nucleic acid that hybridizes to the "DNA MISMATCH REPAIR PROTEIN MSH6" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "DNA-DEPENDENT PROTEIN KINASE CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" encoded by a nucleic acid that hybridizes to the "DNA-DIRECTED RNA POLYMERASE II 23 KDA POLYPEPTIDE" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "ELONGATION FACTOR 2 KINASE" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELONGATION FACTOR 2 KINASE" encoded by a nucleic acid that hybridizes to the "ELONGATION FACTOR 2 KINASE" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "FK506-BINDING PROTEIN 4" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FK506-BINDING PROTEIN 4" encoded by a nucleic acid that hybridizes to the "FK506-BINDING PROTEIN 4" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" encoded by a nucleic acid that hybridizes to the "GLIAL FIBRILLARY ACIDIC PROTEIN, ASTROCYTE" nucleic acid or its complement under low stringency conditions, and/or (xxi) "HDCMD34P" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDCMD34P"

encoded by a nucleic acid that hybridizes to the "HDCMD34P" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" encoded by a nucleic acid that hybridizes to the "HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN H" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" encoded by a nucleic acid that hybridizes to the "HISTONE ACETYLTRANSFERASE TYPE B SUBUNIT 2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "HSPC029" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC029" encoded by a nucleic acid that hybridizes to the "HSPC029" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN KIAA0310 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xxvi) "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "INCOMPATIBILITY PROTEIN HET-E-1 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xxvii) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "KIAA1284 PROTEIN (FRAGMENT)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "KIAA1284 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1284 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "MEPRIN A BETA-SUBUNIT PRECURSOR" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEPRIN A BETA-SUBUNIT PRECURSOR" encoded by a nucleic acid that hybridizes to the "MEPRIN A BETA-SUBUNIT PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "MUTS" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MUTS" encoded by a nucleic acid that hybridizes to the "MUTS" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "MYELOID LEUKEMIA FACTOR 2" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MYELOID LEUKEMIA FACTOR 2" encoded by a nucleic acid that hybridizes to the "MYELOID LEUKEMIA FACTOR 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" encoded by a nucleic acid that hybridizes to the "NEIGHBOR OF A-KINASE ANCHORING PROTEIN 95" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "P30 DBC" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P30 DBC" encoded by a nucleic acid that hybridizes to the "P30 DBC" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" encoded by a nucleic acid that hybridizes to the "PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLASE FAF-X" nucleic acid or its complement under low stringency conditions, and/or

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(xxxv) "PROGRAMED CELL DEATH PROTEIN 2" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROGRAMED CELL DEATH PROTEIN 2" encoded by a nucleic acid that hybridizes to the "PROGRAMED CELL DEATH PROTEIN 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "PROLIFERATING CELL NUCLEAR ANTIGEN" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROLIFERATING CELL NUCLEAR ANTIGEN" encoded by a nucleic acid that hybridizes to the "PROLIFERATING CELL NUCLEAR ANTIGEN" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "PROTEASOME SUBUNIT BETA TYPE 3" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROTEASOME SUBUNIT BETA TYPE 3" encoded by a nucleic acid that hybridizes to the "PROTEASOME SUBUNIT BETA TYPE 3" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Pot1" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pot1" encoded by a nucleic acid that hybridizes to the "Pot1" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "RAD50 HOMOLOGUE HSRAD50" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAD50 HOMOLOGUE HSRAD50" encoded by a nucleic acid that hybridizes to the "RAD50 HOMOLOGUE HSRAD50" nucleic acid or its complement under low stringency conditions, and/or

- (xl) "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" encoded by a nucleic acid that hybridizes to the "RAS GTPASE-ACTIVATING-LIKE PROTEIN IQGAP2" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" encoded by a nucleic

acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-ALPHA 1 CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

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(xlii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-BETA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" encoded by a nucleic acid that hybridizes to the "SERINE/THREONINE PROTEIN PHOSPHATASE PP1-GAMMA CATALYTIC SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or

- (xliv) "SIMILAR TO OROSOMUCOID 1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO OROSOMUCOID 1" encoded by a nucleic acid that hybridizes to the "SIMILAR TO OROSOMUCOID 1" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "SMC5 PROTEIN" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMC5 PROTEIN" encoded by a nucleic acid that hybridizes to the "SMC5 PROTEIN" nucleic acid or its complement under low stringency conditions, and/or
- (xlvi) "SQUAMOUS CELL CARCINOMA ANTIGEN 1" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SQUAMOUS CELL CARCINOMA ANTIGEN 1" encoded by a nucleic acid that hybridizes to the "SQUAMOUS CELL CARCINOMA ANTIGEN 1" nucleic acid or its complement under low stringency conditions, and/or
- (xlvii) "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG"

encoded by a nucleic acid that hybridizes to the "SUPPRESSOR OF G2 ALLELE OF SKP1 HOMOLOG" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" encoded by a nucleic acid that hybridizes to the "Serine/threonine proteine phosphatase 2A, catalytic subunit, beta isoform" nucleic acid or its complement under low stringency conditions, and/or

- (xlix) "Similar to diacylglycerol kinase delta" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to diacylglycerol kinase delta" encoded by a nucleic acid that hybridizes to the "Similar to diacylglycerol kinase delta" nucleic acid or its complement under low stringency conditions, and/or
- (I) "TELOMERASE-BINDING PROTEIN P23" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERASE-BINDING PROTEIN P23" encoded by a nucleic acid that hybridizes to the "TELOMERASE-BINDING PROTEIN P23" nucleic acid or its complement under low stringency conditions, and/or
- (Ii) "TELOMERIC REPEAT BINDING FACTOR 2" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TELOMERIC REPEAT BINDING FACTOR 2" encoded by a nucleic acid that hybridizes to the "TELOMERIC REPEAT BINDING FACTOR 2" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" encoded by a nucleic acid that hybridizes to the "TERF1 (TRF1)-INTERACTING NUCLEAR FACTOR 2" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "TRF1" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF1" encoded by a nucleic acid that hybridizes to the "TRF1" nucleic acid or its complement under low stringency conditions, and/or

- (liv) "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" encoded by a nucleic acid that hybridizes to the "TRF2-INTERACTING TELOMERIC RAP1 PROTEIN" nucleic acid or its complement under low stringency conditions, and/or (Iv) "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" encoded by a nucleic acid that hybridizes to the "TRICARBOXYLATE TRANSPORT PROTEIN, MITOCHONDRIAL PRECURSOR" nucleic acid or its complement under low stringency conditions, and/or (Ivi) "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "U5 SMALL NUCLEAR RIBONUCLEOPROTEIN 200 KDA HELICASE (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (Ivii) "WD-REPEAT PROTEIN AN11 HOMOLOG" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "WD-REPEAT PROTEIN AN11 HOMOLOG" encoded by a nucleic acid that hybridizes to the "WD-REPEAT PROTEIN AN11 HOMOLOG" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as cancer such as solid tumours such as breast cancer, prostate cancer, lung cancer, colon cancer; cancer such as haematological cancers such as leukemia.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as cancer such as solid tumours such as breast cancer, prostate cancer, lung cancer, colon cancer; cancer such as haematological cancers such as leukemia.

- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "38 KDA FK-506 BINDING PROTEIN HOMOLOG" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "38 KDA FK-506 BINDING PROTEIN HOMOLOG" encoded by a nucleic acid that hybridizes to the "38 KDA FK-506 BINDING PROTEIN HOMOLOG" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "ANTIGEN NY-CO-7" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ANTIGEN NY-CO-7" encoded by a nucleic acid that hybridizes to the "ANTIGEN NY-CO-7" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" encoded by a nucleic acid that hybridizes to the "ATP-BINDING CASSETTE, SUB-FAMILY D, MEMBER 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "ATP-DEPENDENT DNA HELICASE II, 80 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BAF180" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAF180" encoded by a nucleic acid that hybridizes to the "BAF180" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "CASEIN KINASE II, ALPHA CHAIN" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CASEIN KINASE II, ALPHA CHAIN" encoded by a nucleic acid that hybridizes to the "CASEIN KINASE II, ALPHA CHAIN" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CDNA FLJ13664 FIS, CLONE PLACE1011649" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13664 FIS, CLONE PLACE1011649" encoded by a nucleic

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acid that hybridizes to the "CDNA FLJ13664 FIS, CLONE PLACE1011649" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "CDNA FLJ13998 FIS, CLONE Y79AA1002229" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ13998 FIS, CLONE Y79AA1002229" encoded by a nucleic acid that hybridizes to the "CDNA FLJ13998 FIS, CLONE Y79AA1002229" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "CDNA FLJ20643 FIS, CLONE KAT02633" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ20643 FIS, CLONE KAT02633" encoded by a nucleic acid that hybridizes to the "CDNA FLJ20643 FIS, CLONE KAT02633" nucleic acid or its complement under low stringency conditions, and/or
- (x) "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "CDNA FLJ25320 FIS, CLONE TST00267 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "CDNA FLJ31741 FIS, CLONE NT2RI2007148" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA FLJ31741 FIS, CLONE NT2RI2007148" encoded by a nucleic acid that hybridizes to the "CDNA FLJ31741 FIS, CLONE NT2RI2007148" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "CDNA: FLJ21908 FIS, CLONE HEP03830" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDNA: FLJ21908 FIS, CLONE HEP03830" encoded by a nucleic acid that hybridizes to the "CDNA: FLJ21908 FIS, CLONE HEP03830" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "CENP-F KINETOCHORE PROTEIN" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CENP-F KINETOCHORE PROTEIN" encoded by a nucleic acid that hybridizes to the "CENP-F KINETOCHORE PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

variant of "HYPOTHETICAL 68.1 KDA PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL 68.1 KDA PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxv) "HYPOTHETICAL PROTEIN XP_058906" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_058906" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_058906" nucleic acid or its complement under low stringency conditions,

(xxvi) "Heat shock protein 90, alpha" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Heat shock protein 90, alpha" encoded by a nucleic acid that hybridizes to the "Heat shock protein 90, alpha" nucleic acid or its complement under low stringency conditions, (xxvii) "Her2" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Her2" encoded by a nucleic acid that hybridizes to the "Her2" nucleic acid or its complement under low stringency conditions,

(xxviii) "Her4" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Her4" encoded by a nucleic acid that hybridizes to the "Her4" nucleic acid or its complement under low stringency conditions,

(xxix) "INSULIN RECEPTOR SUBSTRATE 4" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "INSULIN RECEPTOR SUBSTRATE 4" encoded by a nucleic acid that hybridizes to the "INSULIN RECEPTOR SUBSTRATE 4" nucleic acid or its complement under low stringency conditions,

(xxx) "KIAA0667 PROTEIN (FRAGMENT)" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0667 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0667 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxi) "KIAA0792 PROTEIN" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0792 PROTEIN" encoded by a nucleic acid that hybridizes to the "KIAA0792 PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxxii) "KIAA0887 PROTEIN (FRAGMENT)" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0887 PROTEIN (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0887 PROTEIN (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxiii) "PALMITOYL-PROTEIN THIOESTERASE 1 PRECURSOR" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PALMITOYL-PROTEIN THIOESTERASE 1 PRECURSOR" encoded by a nucleic acid that hybridizes to the "PALMITOYL-PROTEIN THIOESTERASE 1 PRECURSOR" nucleic acid or its complement under low stringency conditions,

(xxxiv) "PI3 kinase regulatory subunit p55 gamma" (SEQ ID No.90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PI3 kinase regulatory subunit p55 gamma" encoded by a nucleic acid that hybridizes to the "PI3 kinase regulatory subunit p55 gamma" nucleic acid or its complement under low stringency conditions,

(xxxv) "PI3 kinase regulatory subunit p85 alpha" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PI3 kinase regulatory subunit p85 alpha" encoded by a nucleic acid that hybridizes to the "PI3 kinase regulatory subunit p85 alpha" nucleic acid or its complement under low stringency conditions,

(xxxvi) "PI3 kinase regulatory subunit p85 beta" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PI3 kinase regulatory subunit p85 beta" encoded by a nucleic acid that hybridizes to the "PI3 kinase regulatory subunit p85 beta" nucleic acid or its complement under low stringency conditions,

(xxxvii) "PROCOLLAGEN-PROLINE, 2-OXOGLUTARATE 4-DIOXYGENASE (PROLINE 4- HYDROXYLASE), ALPHA POLYPEPTIDE I" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PROCOLLAGEN-PROLINE, 2-OXOGLUTARATE 4-DIOXYGENASE (PROLINE 4- HYDROXYLASE), ALPHA POLYPEPTIDE I" encoded by a nucleic acid that hybridizes to the "PROCOLLAGEN-PROLINE, 2-OXOGLUTARATE 4-DIOXYGENASE (PROLINE 4- HYDROXYLASE), ALPHA POLYPEPTIDE I" nucleic acid or its complement under low stringency conditions,

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Val Asn Thr Lys Pro Glu Lys Thr Glu Glu Asp Ser Glu Glu Val Arg

130

140

Glu Gln Lys His Lys Thr Phe Val Glu Lys Tyr Glu Lys Gln Ile Lys 145 150 155 160 His Phe Gly Met Leu Arg Arg Trp Asp Asp Ser Gln Lys Tyr Leu Ser 165 170 175 Asp Asn Val His Leu Val Cys Glu Glu Thr Ala Asn Tyr Leu Val Ile 180 185 190 Trp Cys Ile Asp Leu Glu Val Glu Glu Lys Cys Ala Leu Met Glu Gln 195 200 205 Val Ala His Gin Thr Ile Val Met Gin Phe Ile Leu Glu Leu Ala Lys 210 215 220 Ser Leu Lys Val Asp Pro Arg Ala Cys Phe Arg Gln Phe Phe Thr Lys 225 230 235 240 Ile Lys Thr Ala Asp Arg Gln Tyr Met Glu Gly Phe Asn Asp Glu Leu 245 250 255 Glu Ala Phe Lys Glu Arg Val Arg Gly Arg Ala Lys Leu Arg Ile Glu 260 265 270 Lys Ala Met Lys Glu Tyr Glu Glu Glu Glu Arg Lys Lys Arg Leu Gly 275 280 285 Pro Gly Gly Leu Asp Pro Val Glu Val Tyr Glu Ser Leu Pro Glu Glu 290 295 300 Leu Gln Lys Cys Phe Asp Val Lys Asp Val Gln Met Leu Gln Asp Ala 305 310 315 Ile Ser Lys Met Asp Pro Thr Asp Ala Lys Tyr His Met Gln Arg Cys 325 330 335Ile Asp Ser Gly Leu Trp Val Pro Asn Ser Lys Ala Ser Glu Ala Lys 345 Glu Gly Glu Ala Gly Pro Gly Asp Pro Leu Leu Glu Ala Val Pro 355 360 Lys Thr Gly Asp Glu Lys Asp Val Ser Val

<210> 63 <211> 237 <212> PRT

213> Homo sapiens

<400> 63

Met Ala Glu Ala Leu Gly Val Ser Val Thr Asp Tyr Thr Phe Glu Asp 15

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Cys Leu Leu Glu Phe Ala Arg Leu Val Arg Gly Leu Gly Leu Lys Pro 45

Glu Lys Leu Glu Lys Asp Leu Asp Arg Tyr Ser Glu Arg Ala Arg Met 50 60

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Gly Gly Glu Lys Ile Gly Ile Ala Glu Phe Ala Ala Ser Leu Glu 65 70 75 80 Val Pro Val Ser Asp Leu Leu Glu Asp Met Phe Ser Leu Phe Asp Glu 85 90 95 Ser Gly Ser Gly Glu Val Asp Leu Arg Glu Cys Val Val Ala Leu Ser Val Val Cys Arg Pro Ala Arg Thr Leu Asp Thr Ile Gln Leu Ala Phe 115 125Lys Thr Tyr Gly Ala Gln Glu Asp Gly Ser Val Gly Glu Gly Asp Leu 130 140Ser Cys Ile Leu Lys Thr Ala Leu Gly Val Ala Glu Leu Thr Val Thr 145 150 155 160 Asp Leu Phe Arg Ala Ile Asp Gln Glu Glu Lys Gly Lys Ile Thr Phe 165 170 175Ala Asp Phe His Arg Phe Ala Glu Met Tyr Pro Ala Phe Ala Glu Glu 180 185 190 Tyr Leu Tyr Pro Asp Gln Thr His Phe Glu Ser Cys Ala Glu Thr Ser 195 200 205 Pro Ala Pro Ile Pro Asn Gly Phe Cys Ala Asp Phe Ser Pro Glu Asn 210 225 Ser Asp Ala Gly Arg Lys Pro Val Arg Lys Leu Asp 225 230 235

<210> 64 <211> 568 <212> PRT <213> Homo sapiens

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Leu Ala Leu Leu Gly Leu Gly Ile Ser Ser Phe Val Leu Ile Thr Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 130 135

PCT/EP2003/007835

Cys Ala Asn Met Leu Leu Met Ala Ala Leu Trp Gly Leu Tyr Met Ser 145 155 160 Leu Val Asn Val Gly His Val Trp Glu Ala Glu Ala Arg Trp Glu Ser 165 170 175 Gln Leu Leu Glu Thr Gly Phe Leu Gly Ile Phe Leu Cys Pro Leu Trp
180 185 190 Thr Leu Ser Arg Leu Pro Gln His Thr Pro Thr Ser Arg Ile Val Leu 195 200 205 Trp Gly Phe Arg Trp Leu Ile Phe Arg Ile Met Leu Gly Ala Gly Leu 210 215 220 Ile Lys Ile Arg Gly Asp Arg Cys Trp Arg Asp Leu Thr Cys Met Asp Phe His Tyr Glu Thr Gln Pro Met Pro Asn Pro Val Ala Tyr Tyr Leu 245 250 255 His His Ser Pro Trp Trp Phe His Arg Phe Glu Thr Leu Ser Asn His 260 265 270 Phe Ile Glu Leu Leu Val Pro Phe Phe Leu Phe Leu Gly Arg Arg Ala 275 280 285 Cys Ile Ile His Gly Val Leu Gln Ile Leu Phe Gln Ala Val Leu Ile Val Ser Gly Asn Leu Ser Phe Leu Asn Trp Leu Thr Met Val Pro Ser 305 310 315 320 Leu Ala Cys Phe Asp Asp Ala Thr Leu Gly Phe Leu Phe Pro Ser Gly 325 330 Pro Gly Ser Leu Lys Asp Arg Val Leu Gln Met Gln Arg Asp Ile Arg 340 345 350 Gly Ala Arg Pro Glu Pro Arg Phe Gly Ser Val Val Arg Arg Ala Ala Asn Val Ser Leu Gly Val Leu Leu Ala Trp Leu Ser Val Pro Val Val 370 380 Leu Asn Leu Leu Ser Ser Arg Gln Val Met Asn Thr His Phe Asn Ser 385 390 395 400 Leu His Ile Val Asn Thr Tyr Gly Ala Phe Gly Ser Ile Thr Lys Glu 405 410 415 Arg Ala Glu Val Ile Leu Gln Gly Thr Ala Ser Ser Asn Ala Ser Ala 420 425 430 Pro Asp Ala Met Trp Glu Asp Tyr Glu Phe Lys Cys Lys Pro Gly Asp 440 445 Pro Ser Arg Arg Pro Cys Leu Ile Ser Pro Tyr His Tyr Arg Leu Asp 450 460 Trp Leu Met Trp Phe Ala Ala Phe Gln Thr Tyr Glu His Asn Asp Trp

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ile Ile His Leu Ala Gly Lys Leu Leu Ala Ser Asp Ala Glu Ala Leu
485
490
495

Ser Leu Leu Ala His Asn Pro Phe Ala Gly Arg Pro Pro Pro Arg Trp Val Arg Gly Glu His Tyr Arg Tyr Lys Phe Ser Arg Pro Gly Gly Arg S15 Gly Ala Tyr Arg S20 Fro Pro Pro Leu Ser Leu Glu Glu Leu Arg Pro Tyr Phe Arg Asp Arg S60 Gly Trp Pro Leu Pro Gly Pro Leu

<210> 65

<211> 764 <212> PRT

<213> Homo sapiens

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Asp Val Tyr Glu Thr Lys Cys Cys His Gln Val Trp Glu Met Asn 235 230 235 Met Asp Gln Leu Leu Leu Val Ala Asp Leu Trp Arg Tyr Leu Gly Arg 250 255 Lys Val Pro Arg Phe Leu Asn Ile Phe Ser Ser Tyr Leu Asn Leu His 260 265 270 Trp Lys Asp Leu Ser Leu Ser Gln Leu Val His Leu Ile Tyr Val Ile 275 280 285 Gly Glu Asn Arg Gln Val Ser Gln Asp Leu Met Gln Lys Leu Glu Ser 290 300 Leu Ile Leu Lys Tyr Ile Asp Leu Ile Asn Leu Glu Glu Val Gly Thr Ile Cys Leu Gly Phe Phe Lys Ser Ser Thr Asn Leu Ser Glu Phe Val Met Arg Lys Ile Gly Asp Leu Ala Cys Ala Asn Ile Gln His Leu Ser 340 345 350 Ser Arg Ser Leu Val Asn Ile Val Lys Met Phe Arg Phe Thr His Val Asp His Ile Asn Phe Met Lys Gln Ile Gly Glu Ile Ala Pro Gln Arg 370 380Ile Pro Ser Leu Gly Val Gl
n Gly Val Met His Leu Thr Leu Tyr Cys 385 390395 Ser Ala Leu Arg Phe Leu Asn Glu Gly Val Met Asn Ala Val Ala Ala 410 415 Ser Leu Pro Pro Arg Val Ala His Cys Arg Ser Lys Asp Val Ala Lys 420 425 430 Ile Leu Trp Ser Phe Gly Thr Leu Asn Tyr Lys Pro Pro Asn Ala Glu . 435 440 445 Glu Phe Tyr Ser Ser Leu Ile Ser Glu Ile His Arg Lys Met Pro Glu 450 455 460 Phe Asn Gln Tyr Pro Glu His Leu Pro Thr Cys Leu Leu Gly Leu Ala 465 470 475 480 Phe Leu Glu Tyr Phe Pro Val Glu Leu Ile Asp Phe Ala Leu Ser Pro 485 490 495 Gly Phe Val Arg Leu Ala Gln Glu Arg Thr Lys Phe Asp Leu Leu Lys 500 505 510 Glu Leu Tyr Thr Leu Asp Gly Thr Val Gly Ile Glu Cys Pro Asp Tyr 515 525 Arg Gly Asn Arg Leu Ser Thr His Leu Gln Gln Glu Gly Ser Glu Leu 530 540 Leu Trp Tyr Leu Ala Glu Lys Asp Met Asn Ser Lys Pro Glu Phe Leu 545 550 560

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Thr Val Phe Leu Leu Glu Thr Met Leu Gly Gly Pro Gln Tyr Val
565 570 575

Lys His His Met Ile Leu Pro His Thr Arg Ser Ser Asp Leu Glu Val 580 585 590 Gln Leu Asp Val Asn Leu Lys Pro Leu Pro Phe Asn Arg Glu Ala Thr 595 600 605Pro Ala Glu Asn Val Ala Lys Leu Arg Leu Glu His Val Gly Val Ser 610 620 Leu Thr Asp Asp Leu Met Asn Lys Leu Leu Lys Gly Lys Ala Arg Gly 625 630 635 His Phe Gln Gly Lys Thr Glu Ser Glu Pro Gly Gln Gln Pro Met Glu 645 650 655 Leu Glu Asn Lys Ala Ala Val Pro Leu Gly Gly Phe Leu Cys Asn Val 660 665 670 Ala Asp Lys Ser Gly Ala Met Glu Met Ala Gly Leu Cys Pro Ala Ala 675 680 Cys Met Gln Thr Pro Arg Met Lys Leu Ala Val Gln Phe Thr Asn Arg $690 \hspace{1.5cm} 695 \hspace{1.5cm} 700$ Asn Gln Tyr Cys Tyr Gly Ser Arg Asp Leu Leu Gly Leu His Asn Met 705 710 715 720 Lys Arg Arg Gln Leu Ala Arg Leu Gly Tyr Arg Val Val Glu Leu Ser 725 730 735 Tyr Trp Glu Trp Leu Pro Leu Leu Lys Arg Thr Arg Leu Glu Lys Leu 745 750 Ala Phe Leu His Glu Lys Val Phe Thr Ser Ala Leu

66 355 PRT Homo sapiens

Met Ser Thr Asn Gly Val Ser Asn Gly Val Ser Asn Gly Leu His Leu 1 10 15 His Ser Asn Gly Phe Arg Leu Pro Glu Ser Arg Gly His Val Ser Pro 20 30 Gln Val Glu Leu Pro Pro Tyr Leu Glu Arg Val Lys Gln Gln Ala Asn 35 40 45Glu Ala Phe Ala Cys Gln Gln Trp Thr Gln Ala Ile Gln Leu Tyr Ser Lys Ala Val Gln Arg Ala Pro His Asn Ala Met Leu Tyr Gly Asn Arg 65 70 75 80

Leu Arg Asp Cys Leu Lys Ala Ile Ser Leu Asn Pro Cys His Leu Lys

Ala Ala Ala Tyr Met Lys Arg Lys Trp Asp Gly Asp His Tyr Asp Ala 90 95

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ala His Phe Arg Leu Ala Arg Cys Leu Phe Glu Leu Lys Tyr Val Ala

115 120 125

Glu Ala Leu Glu Cys Leu Asp Asp Phe Lys Gly Lys Phe Pro Glu Gln 130 140 Ala His Ser Ser Ala Cys Asp Ala Leu Gly Arg Ala Ile Thr Ala Ala 145 150 160 Leu Phe Ser Lys Asn Asp Gly Glu Glu Lys Lys Gly Pro Gly Gly Gly 175 Ala Pro Val Arg Leu Arg Ser Thr Ser Arg Lys Asp Ser Ile Ser Glu $180 \hspace{1cm} 185 \hspace{1cm} 190 \hspace{1cm}$ Asp Glu Met Ala Leu Arg Glu Arg Ser Tyr Asp Tyr Gln Phe Arg Tyr 195 200 205 Cys Gly His Cys Asn Thr Thr Thr Asp Ile Lys Glu Ala Asn Phe Phe 210 215 220Gly Ser Asn Ala Gln Tyr Ile Val Ser Gly Ser Asp Asp Gly Ser Phe Phe Ile Trp Glu Lys Glu Thr Thr Asn Leu Val Arg Val Leu Gln Gly
245 250 255 Asp Glu Ser Ile Val Asn Cys Leu Gln Pro His Pro Ser Tyr Cys Phe 260 265 270 Leu Ala Thr Ser Gly Ile Asp Pro Val Val Arg Leu Trp Asn Pro Arg 275 280 285 Pro Glu Ser Glu Asp Leu Thr Gly Arg Val Val Glu Asp Met Glu Gly 290 295 300 Ala Ser Gln Ala Asn Gln Arg Arg Met Asn Ala Asp Pro Leu Glu Val 305 310 320 Met Leu Leu Asn Met Gly Tyr Arg Ile Thr Gly Leu Ser Ser Gly Gly 325 330 335 Ala Gly Ala Ser Asp Asp Glu Asp Ser Ser Glu Gly Gln Val Gln Cys 340 350

Arg Pro Ser 355

<210> 67

<212> PRT <213> Homo sapiens

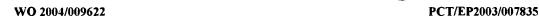
<400> 67

Met Gln Ser Lys Met Arg Ser Tyr Gln Ala Lys Val Arg Gln Gly Ala 1 10 15

Leu val Cys Phe Leu Ser Thr Ile Lys Ser Ile Glu Lys Lys Val Leu $20 \hspace{1cm} 25 \hspace{1cm} 30$

Tyr Gly Tyr Trp Ser Ala Phe Ile Pro Asp Thr Pro Glu Leu Gly Ser

Pro Gln Ser Val Ser Leu Met Thr Leu Thr Leu Lys Asp Pro Ser Pro 50 $\,$



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Thr Arg Ala Cys Ala Leu Gln Val Leu Ser Ala Ile Leu Glu Gly Ser Lys Gln Phe Leu Ser Val Ala Glu Asp Thr Ser Asp His Arg Arg Ala Phe Thr Pro Phe Ser Val Met Ile Ala Cys Ser Ile Arg Glu Leu 100 105 110 His Arg Cys Leu Leu Leu Ala Leu Val Ala Glu Ser Ser Gln Thr 115 120 125 val Thr Gln Ile Ile Lys Cys Leu Ala Asn Leu Val Ser Asn Ala Pro 130 135 140 Tyr Asp Arg Leu Lys Leu Ser Leu Leu Thr Lys Val Trp Asn Gln Ile 145 150 155 160 Lys Pro Tyr Ile Arg His Lys Asp Val Asn Val Arg Val Ser Ser Leu 165 170 175 Thr Leu Leu Gly Ala Ile Val Ser Thr His Ala Pro Leu Pro Glu Val $180 \hspace{1cm} 185 \hspace{1cm} 190$ Gln Leu Leu Gln Gln Pro Cys Ser Ser Gly Leu Gly Asn Ser Asn 195 200 205 Ser Ala Thr Pro His Leu Ser Pro Pro Asp Trp Trp Lys Lys Thr Pro 210 220 Ala Gly Pro Ser Leu Glu Glu Thr Ser Val Ser Ser Pro Lys Gly Ser 275 230 235 240 Ser Glu Pro Cys Trp Leu Ile Arg Leu Cys Ile Ser Ile Val Val Leu 245 250 255 Pro Lys Glu Asp Ser Cys Ser Gly Ser Asp Ala Gly Ser Ala Ala Gly 260 265 270 Ser Thr Tyr Glu Pro Ser Pro Met Arg Leu Glu Ala Leu Gln Val Leu 275 280 285 Thr Leu Leu Ala Arg Gly Tyr Phe Ser Met Thr Gln Ala Tyr Leu Met Glu Leu Gly Glu Val Ile Cys Lys Cys Met Gly Glu Ala Asp Pro Ser 305 310 315 Ile Gln Leu His Gly Ala Lys Leu Leu Glu Glu Leu Gly Thr Gly Leu 325 330 335 Ile Gln Gln Tyr Lys Pro Asp Ser Thr Ala Ala Pro Asp Gln Arg Ala 340 345 350 Pro val Phe Leu val Val Met Phe Trp Thr Met Met Leu Asn Gly Pro 355 360 365 Leu pro Arg Ala Leu Gln Asn Ser Glu His Pro Thr Leu Gln Ala Ser 370 375 380 Ala Cys Asp Ala Leu Ser Ser Ile Leu Pro Glu Ala Phe Ser Asn Leu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Pro Asn Asp Arg Gln Met Leu Cys Ile Thr Val Leu Leu Gly Leu Asn 405 410 415

Asp Ser Lys Asn Arg Leu Val Lys Ala Ala Thr Ser Arg Ala Leu Gly 425 430 Val Tyr Val Leu Phe Pro Cys Leu Arg Gln Asp Val Ile Phe Val Ala 435 440 445 Asp Ala Ala Asn Ala Ile Leu Met Ser Leu Glu Asp Lys Ser Leu Asn 450 455 460 Val Arg Ala Lys Ala Ala Trp Ser Leu Gly Asn Leu Thr Asp Thr Leu
465 470 480 Ile Val Asn Met Glu Thr Pro Asp Pro Ser Phe Gln Glu Glu Phe Ser 490 495 Gly Leu Leu Leu Lys Met Leu Arg Ser Ala Ile Glu Ala Ser Lys 500 505 510 Asp Lys Asp Lys Val Lys Ser Asn Ala Val Arg Ala Leu Gly Asn Leu 515 525 Leu His Phe Leu Gln Pro Ser His Ile Glu Lys Pro Thr Phe Ala Glu 530 535 540 Ile Ile Glu Glu Ser Ile Gln Ala Leu Ile Ser Thr Val Leu Thr Glu 545 550 555 560 Ala Ala Met Lys Val Arg Trp Asn Ala Cys Tyr Ala Met Gly Asn Val Phe Lys Asn Pro Ala Leu Pro Leu Gly Thr Ala Pro Trp Thr Ser Gln 580 585 590 Ala Tyr Asn Ala Leu Thr Ser Val Val Thr Ser Cys Lys Asn Phe Lys $595 \hspace{1.5cm} 600 \hspace{1.5cm} 605$ Val Arg Ile Arg Ser Ala Ala Ala Leu Ser Val Pro Gly Lys Arg Glu 610 620 Gln Tyr Gly Ser Val Asp Gln Tyr Ala Arg Ile Trp Asn Ala Leu Val 625 630 640 Thr Ala Leu Gln Lys Ser Glu Asp Thr Ile Asp Phe Leu Glu Phe Lys 645 650 655 Tyr Cys Val Ser Leu Arg Thr Gln Ile Cys Gln Ala Leu Ile His Leu 660 665 670 Leu Ser Leu Ala Ser Ala Ser Asp Leu Pro Cys Met Lys Glu Thr Leu 675 680 Glu Leu Ser Gly Asn Met Val Gln Ser Tyr Ile Leu Gln Phe Leu Lys 690 695 700 Ser Gly Ala Glu Gly Asp Asp Thr Gly Ala Pro His Ser Pro Gln Glu 705 710 715 720 Arg Asp Gln Met Val Arg Met Ala Leu Lys His Met Gly Ser Ile Gln 730 730Ala Pro Thr Gly Asp Thr Ala Arg Arg Ala Ile Met Gly Phe Leu Glu Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Ile Leu Ala Val Cys Phe Asp Ser Ser Gly Ser Gln Gly Ala Leu 755 760 765 Pro Gly Leu Thr Asn Gln 770

68 213 PRT Homo sapiens <400> 68 Met Pro Asp Glu Asn Ile Phe Leu Phe Val Pro Asn Leu Ile Gly Tyr 1 10 15 Ala Arg Ile Val Phe Ala Ile Ile Ser Phe Tyr Phe Met Pro Cys Cys Pro Leu Thr Ala Ser Ser Phe Tyr Leu Leu Ser Gly Leu Leu Asp Ala 35 40 45Phe Asp Gly His Ala Ala Arg Ala Leu Asn Gln Gly Thr Arg Phe Gly 50 60 Ala Met Leu Asp Met Leu Thr Asp Arg Cys Ser Thr Met Cys Leu Leu 65 70 80 val Asn Leu Ala Leu Leu Tyr Pro Gly Ala Thr Leu Phe Phe Gln Ile $85\,$ Ser Met Ser Leu Asp Val Ala Ser His Trp Leu His Leu His Ser Ser 100 105 110Val Val Arg Gly Ser Glu Ser His Lys Met Ile Asp Leu Ser Gly Asn 115 120 Pro Val Leu Arg Ile Tyr Tyr Thr Ser Arg Pro Ala Leu Phe Thr Leu Cys Ala Gly Asn Glu Leu Phe Tyr Cys Leu Leu Tyr Leu Phe His Phe 145 150 160 Ser Glu Gly Pro Leu Val Gly Ser Val Gly Leu Phe Arg Met Gly Leu 165 170 175 Trp Val Thr Ala Pro Ile Ala Leu Leu Lys Ser Leu Ile Ser Val Ile 180 185 190 His Leu Ile Thr Ala Ala Arg Asn Met Ala Ala Leu Asp Ala Ala Asp 195 200 205

<210> 69 <211> 1047 <212> PRT <213> Homo sapiens

Arg Ala Lys Lys Lys 210

<400> 69

Met ala Val Thr Leu Asp Lys Asp Ala Tyr Tyr Arg Arg Val Lys Arg 1 10 15

Leu Tyr Ser Asn Trp Arg Lys Gly Glu Asp Glu Tyr Ala Asn Val Asp

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Ile Val Val Ser Val Gly Val Asp Glu Glu Ile Val Tyr Ala Lys Ser Thr Ala Leu Gln Thr Trp Leu Phe Gly Tyr Glu Leu Thr Asp Thr Ile Met Val Phe Cys Asp Asp Lys Ile Ile Phe Met Ala Ser Lys Lys Lys Val Glu Phe Leu Lys Gln Ile Ala Asn Thr Lys Gly Asn Glu Asn 90 95 Ala Asn Gly Ala Pro Ala Ile Thr Leu Leu Ile Arg Glu Lys Asn Glu 100 105 110 Ser Asn Lys Ser Ser Phe Asp Lys Met Ile Glu Ala Ile Lys Glu Ser 115 120 125Lys Asn Gly Lys Lys Ile Gly Val Phe Ser Lys Asp Lys Phe Pro Gly 130 140 Glu Phe Met Lys Ser Trp Asn Asp Cys Leu Asn Lys Glu Gly Phe Asp 145 150 155 160 Lys Ile Asp Ile Ser Ala Val Val Ala Tyr Thr Ile Ala Val Lys Glu 165 170 175 Asp Gly Glu Leu Asn Leu Met Lys Lys Ala Ala Ser Ile Thr Ser Glu 180 185 190 Val Phe Asn Lys Phe Phe Lys Glu Arg Val Met Glu Ile Val Asp Ala 195 200 205 Asp Glu Lys Val Arg His Ser Lys Leu Ala Glu Ser Val Glu Lys Ala 210 220 Ile Glu Glu Lys Lys Tyr Leu Ala Gly Ala Asp Pro Ser Thr Val Glu 225 230 240 Met Cys Tyr Pro Pro Ile Ile Gln Ser Gly Gly Asn Tyr Asn Leu Lys 245 250 255 Phe Ser Val Val Ser Asp Lys Asn His Met His Phe Gly Ala Ile Thr 260 265 270 Cys Ala Met Gly Ile Arg Phe Lys Ser Tyr Cys Ser Asn Leu Val Arg 275 280 285 Thr Leu Met Val Asp Pro Ser Gln Glu Val Gln Glu Asn Tyr Asn Phe 290 300 Leu Leu Gln Leu Gln Glu Glu Leu Leu Lys Glu Leu Arg His Gly Val 305 310 315 320 Lys Ile Cys Asp Val Tyr Asn Ala Val Met Asp Val Val Lys Lys Gln 325 330 Lys Pro Glu Leu Leu Asn Lys Ile Thr Lys Asn Leu Gly Phe Gly Met 340 350 Gly Ile Glu Phe Arg Glu Gly Ser Leu Val Ile Asn Ser Lys Asn Gln

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Tyr Lys Leu Lys Lys Gly Met Val Phe Ser Ile Asn Leu Gly Phe Ser
370 380

Asp Leu Thr Asn Lys Glu Gly Lys Lys Pro Glu Glu Lys Thr Tyr Ala 385 390395 Leu Phe Ile Gly Asp Thr Val Leu Val Asp Glu Asp Gly Pro Ala Thr val Leu Thr Ser Val Lys Lys Lys Val Lys Asn Val Gly Ile Phe Leu 420 430 Lys Asn Glu Asp Glu Glu Glu Glu Glu Glu Lys Asp Glu Ala Glu 435 440 445 Asp Leu Leu Gly Arg Gly Ser Arg Ala Ala Leu Leu Thr Glu Arg Thr 450 460 Arg Asn Glu Met Thr Ala Glu Glu Lys Arg Arg Ala His Gln Lys Glu 465 470 475 Leu Ala Ala Gln Leu Asn Glu Glu Ala Lys Arg Arg Leu Thr Glu Gln
485 490 495 Lys Gly Glu Gln Gln Ile Gln Lys Ala Arg Lys Ser Asn Val Ser Tyr $500 \hspace{1.5cm} 505 \hspace{1.5cm} 505$ Lys Asn Pro Ser Leu Met Pro Lys Glu Pro His Ile Arg Glu Met Lys 515 525 Ile Tyr Ile Asp Lys Lys Tyr Glu Thr Val Ile Met Pro Val Phe Gly 530 540 Ile Ala Thr Pro Phe His Ile Ala Thr Ile Lys Asn Ile Ser Met Ser Val Glu Gly Asp Tyr Thr Tyr Leu Arg Ile Asn Phe Tyr Cys Pro Gly 565 570 575 Ser Ala Leu Gly Arg Asn Glu Gly Asn Ile Phe Pro Asn Pro Glu Ala 580 585 590 Thr Phe Val Lys Glu Ile Thr Tyr Arg Ala Ser Asn Ile Lys Ala Pro 595 600 605 Gly Glu Gln Thr Val Pro Ala Leu Asn Leu Gln Asn Ala Phe Arg Ile 610 620 lle Lys Glu Val Gln Lys Arg Tyr Lys Thr Arg Glu Ala Glu Glu Lys 625 630 635 Glu Lys Glu Gly Ile Val Lys Gln Asp Ser Leu Val Ile Asn Leu Asn 650 655 $\mbox{Arg Ser Asn Pro Lys Leu Lys Asp Leu Tyr Ile Arg Pro Asn Ile Ala <math display="inline">660$ 665 670Gln Lys $\underset{675}{\text{Arg}}$ Met Gln Gly Ser Leu Glu Ala His Val $\underset{685}{\text{Asn}}$ Gly Phe Arg Phe Thr Ser Val Arg Gly Asp Lys Val Asp Ile Leu Tyr Asn Asn Ile 690 700 Lys His Ala Leu Phe Gln Pro Cys Asp Gly Glu Met Ile Ile Val Leu 705 710 725 720

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Phe His Leu Lys Asn Ala Ile Met Phe Gly Lys Lys Arg His Thr Asp Val Gln Phe Tyr Thr Glu Val Gly Glu Ile Thr Thr Asp Leu Gly 740 750 Lys His Gln His Met His Asp Arg Asp Asp Leu Tyr Ala Glu Gln Met 755 760 765 Glu Arg Glu Met Arg His Lys Leu Lys Thr Ala Phe Lys Asn Phe Ile Glu Lys Val Glu Ala Leu Thr Lys Glu Glu Leu Glu Phe Glu Val Pro 785 790 795 800 Phe Arg Asp Leu Gly Phe Asn Gly Ala Pro Tyr Arg Ser Thr Cys Leu 805 810 815 Leu Gln Pro Thr Ser Ser Ala Leu Val Asn Ala Thr Glu Trp Pro Pro 820 825 830 Phe Val Val Thr Leu Asp Glu Val Glu Leu Ile His Phe Glu Arg Val Gln Phe His Leu Lys Asn Phe Asp Met Val Ile Val Tyr Lys Asp Tyr 850 855 860 Ser Lys Lys Val Thr Met Ile Asn Ala Ile Pro Val Ala Ser Leu Asp 865 870 875 880 Pro Ile Lys Glu Trp Leu Asn Ser Cys Asp Leu Lys Tyr Thr Glu Gly Val Gln Ser Leu Asn Trp Thr Lys Ile Met Lys Thr Ile Val Asp Asp 900 910 Pro Glu Gly Phe Phe Glu Gln Gly Gly Trp Ser Phe Leu Glu Pro Glu 915 920 925 Gly Glu Gly Ser Asp Ala Glu Glu Gly Asp Ser Glu Ser Glu Ile Glu 930 940 Asp Glu Thr Phe Asn Pro Ser Glu Asp Asp Tyr Glu Glu Glu Glu Glu 945 950 955 Asp Ser Asp Glu Asp Tyr Ser Ser Glu Ala Glu Glu Ser Asp Tyr Ser 965 970 975 Lys Glu Ser Leu Gly Ser Glu Glu Glu Ser Gly Lys Asp Trp Asp Glu 980 985 990 Leu Glu Glu Glu Ala Arg Lys Ala Asp Arg Glu Ser Arg Tyr Glu Glu 995 1000 1005 Glu Glu Glu Gln Ser Arg Ser Met Ser Arg Lys Arg Lys Ala Ser 1010 1015 1020 Val His Ser Ser Gly Arg Gly Ser Asn Arg Gly Ser Arg His Ser 1025 1030 1035 Ser Ala Pro Pro Lys Lys Lys Arg Lys 1040 1045

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <210> 70 <211> 564

<212><213> Homo sapiens

<400> Met Leu Ala Asn Ser Ala Ser Val Arg Ile Leu Ile Lys Gly Gly Lys 1 10 15 val Val Asn Asp Asp Cys Thr His Glu Ala Asp Val Tyr Ile Glu Asn 20 25 30 Gly Ile Ile Gln Gln Val Gly Arg Glu Leu Met Ile Pro Gly Gly Ala Lys Val Ile Asp Ala Thr Gly Lys Leu Val Ile Pro Gly Gly Ile Asp S0 55 Thr Ser Thr His Phe His Gln Thr Phe Met Asn Ala Thr Cys Val Asp 65 70 75 Ile Ile Gly His Val Leu Pro Asp Lys Glu Thr Ser Leu Val Asp Ala Tyr Glu Lys Cys Arg Gly Leu Ala Asp Pro Lys Val Cys Cys Asp Tyr 115 120 125 Ala Leu His Val Gly Ile Thr Trp Trp Ala Pro Lys Val Lys Ala Glu 130 135 140 Met Glu Thr Leu Val Arg Glu Lys Gly Val Asn Ser Phe Gln Met Phe Met Thr Tyr Lys Asp Leu Tyr Met Leu Arg Asp Ser Glu Leu Tyr Gln 170 175Val Leu His Ala Cys Lys Asp Ile Gly Ala Ile Ala Arg Val His Ala 180 185 190 Glu Asn Gly Glu Leu Val Ala Glu Gly Ala Lys Glu Ala Leu Asp Leu 195 200 205 Gly Ile Thr Gly Pro Glu Gly Ile Glu Ile Ser Arg Pro Glu Glu Leu Glu Ala Glu Ala Thr His Arg Val Ile Thr Ile Ala Asn Arg Thr His 225 230 235 240 Cys Pro Ile Tyr Leu Val Asn Val Ser Ser Ile Ser Ala Gly Asp Val Ile Ala Ala Lys Met Gln Gly Lys Val Val Leu Ala Glu Thr Thr Thr Ala His Ala Thr Leu Thr Gly Leu His Tyr Tyr His Gln Asp Trp 275 280 285 Ser His Ala Ala Ala Tyr Val Thr Val Pro Pro Leu Arg Leu Asp Thr Asn Thr Ser Thr Tyr Leu Met Ser Leu Leu Ala Asn Asp Thr Leu Asn 305 310 315



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ile Val Ala Ser Asp His Arg Pro Phe Thr Thr Lys Gln Lys Ala Met

325

Gly Lys Glu Asp Phe Thr Lys Ile Pro His Gly Val Ser Gly Val Gln

340

340

Asp Arg Met Ser Val Ile Trp Glu Arg Gly Val Val Gly Gly Lys Met 365

Asp Glu Asn Arg Phe Val Ala Val Thr Ser Ser Asn Ala Ser Lys Leu 370

Leu Asn Leu Tyr Pro Arg Lys Gly Arg Ile Ile Pro Gly Ala His Ala 385

Asp Val Val Trp Asp Pro Glu Ala Thr Lys Thr Ile Ser Ala Ser 410 410

Thr Gln val Gln Gly Gly Asp Phe Asn Leu Tyr Glu Asn Met Arg Cys 420 425 430

His Gly val Pro Leu Val Thr Ile Ser Arg Gly Arg Val Val Tyr Glu 435 440 445

Asn Gly Val Phe Met Cys Ala Glu Gly Thr Gly Lys Phe Cys Pro Leu 450

Arg Ser Phe Pro Asp Thr Val Tyr Lys Lys Leu Val Gln Arg Glu Lys 465 470 475 480

Thr Leu Lys Val Arg Gly Val Asp Arg Thr Pro Tyr Leu Gly Asp Val 485 490 495

Ala val val His Pro Gly Lys Lys Glu Met Gly Thr Pro Leu Ala 500 505 510

Asp Thr Pro Thr Arg Pro Val Thr Arg His Gly Gly Met Arg Asp Leu 515 520 525

His Glu Ser Ser Phe Ser Leu Ser Gly Ser Gln Ile Asp Asp His Val

Pro Lys Arg Ala Ser Ala Arg Ile Leu Ala Pro Pro Gly Gly Arg Ser 545 550 560

ser Gly Ile Trp

<210> 71 <211> 564

<212> PKI <213> Homo sapiens

∠400> 71

Met Leu Ala Asn Ser Ala Ser Val Arg Ile Leu Ile Lys Gly Gly Lys 10 10

val val Asn Asp Asp Cys Thr His Glu Ala Asp Val Tyr Ile Glu Asn $20 \ \ 25 \ \ 30$

Gly Ile Ile Gln Gln Val Gly Arg Glu Leu Met Ile Pro Gly Gly Ala 40 45

Lys val lle Asp Ala Thr Gly Lys Leu Val Ile Pro Gly Gly Ile Asp $50 \hspace{1.5cm} \text{60}$

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Ser Thr His Phe His Gln Thr Phe Met Asn Ala Thr Cys Val Asp 65 70 75 80 Asp Phe Tyr His Gly Thr Lys Ala Ala Leu Val Gly Gly Thr Thr Met Ile Ile Gly His Val Leu Pro Asp Lys Glu Thr Ser Leu Val Asp Ala Tyr Glu Lys Cys Arg Gly Leu Ala Asp Pro Lys Val Cys Cys Asp Tyr 115 120 125 Ala Leu His Val Gly Ile Thr Trp Trp Ala Pro Lys Val Lys Ala Glu 130 135 140 Met Glu Thr Leu Val Arg Glu Lys Gly Val Asn Ser Phe Gln Met Phe 145 150 160 Met Thr Tyr Lys Asp Leu Tyr Met Leu Arg Asp Ser Glu Leu Tyr Gln Val Leu His Ala Cys Lys Asp Ile Gly Ala Ile Ala Arg Val His Ala 180 185 190 Glu Asn Gly Glu Leu Val Ala Glu Gly Ala Lys Glu Ala Leu Asp Leu 195 200 205 Gly Ile Thr Gly Pro Glu Gly Ile Glu Ile Ser Arg Pro Glu Glu Leu 210 215 220 Glu Ala Glu Ala Thr His Arg Val Ile Thr Ile Ala Asn Arg Thr His 225 230 235 240 Cys Pro Ile Tyr Leu Val Asn Val Ser Ser Ile Ser Ala Gly Asp Val 245 250 255 Ile Ala Ala Lys Met Gln Gly Lys Val Val Leu Ala Glu Thr Thr 260 265 270 Thr Ala His Ala Thr Leu Thr Gly Leu His Tyr Tyr His Gln Asp Trp 275 280 285 Ser His Ala Ala Tyr Val Thr Val Pro Pro Leu Arg Leu Asp Thr 290 295 300 Asn Thr Ser Thr Tyr Leu Met Ser Leu Leu Ala Asn Asp Thr Leu Asn 305 310 315 320 Ile Val Ala Ser Asp His Arg Pro Phe Thr Thr Lys Gln Lys Ala Met Gly Lys Glu Asp Phe Thr Lys Ile Pro His Gly Val Ser Gly Val Gln
345 350 Asp Arg Met Ser Val Ile Trp Glu Arg Gly Val Val Gly Gly Lys Met 355 360 365 Asp Glu Asn Arg Phe Val Ala Val Thr Ser Ser Asn Ala Ala Lys Leu Leu Asn Leu Tyr Pro Arg Lys Gly Arg Ile Ile Pro Gly Ala Asp Ala

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Asp Val Val Trp Asp Pro Glu Ala Thr Lys Thr Ile Ser Ala Ser
405 410 415

Thr Gln val Gln Gly Gly Asp Phe Asn Leu Tyr Glu Asn Met Arg Cys
His Gly Val Pro Leu Val Thr Ile Ser Arg Gly Arg Val Val Tyr Glu
Asn Gly Val Phe Met Cys Ala Glu Gly Thr Gly Lys Phe Cys Pro Leu
Arg Ser Phe Pro Asp Thr Val Tyr Lys Lys Leu Val Gln Arg Glu Lys
A65 Thr Leu Lys Val Arg Gly Val Asp Arg Thr Pro Tyr Leu Gly Asp Val
Ala Val Val Val His Pro Gly Lys Lys Glu Met Gly Thr Pro Leu Ala
Asp Thr Pro Thr Arg Pro Val Thr Arg His Gly Gly Met Asp Asp Leu
Fis Glu Ser Ser Phe Ser Leu Ser Gly Ser Gln Ile Asp Asp His Val
Pro Lys Arg Ala Ser Ala Arg Ile Leu Ala Pro Pro Gly Gly Arg Ser
Ser Gly Ile Trp

<210> 72

<211> 395 <212> PRT

<213> Homo sapiens

<400> 72

Met Leu Pro Ala val Gly Ser Ala Asp Glu Glu Glu Asp Pro Ala Glu Glu Asp Pro Ala Glu Glu Asp Cys Pro Gly Leu Val Pro Ile Glu Thr Thr Gln Ser Glu Glu Glu Glu Glu Lys Ser Gly Leu Gly Ala Lys Ile Pro Val Thr Ile Ile Thr Gly Tyr Leu Gly Ala Gly Lys Thr Thr Leu Leu Asn Tyr Ile Leu Thr Glu Gln His Ser Lys Arg Val Ala Val Ile Leu Asn Glu Phe Gly Glu Gly Ser Ala Leu Glu Lys Ser Leu Ala Val Ile Leu Asn Glu Phe Gly Glu Gly Ser Ala Leu Glu Lys Ser Leu Ala Val Ser Gln Gly Gly Glu Leu Tyr Glu Glu Trp Leu Glu Leu Arg Asn Gly Cys Leu Cys Cys Ser Val Lys Asp Ser Gly Leu Arg Ala Ile Glu Asn Leu Met Gln Lys Lys Gly Lys Phe Asp Tyr Ile Leu Leu Glu Thr Thr Gly Leu Ala Asp Pro Gly



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Val Ala Ser Met Phe Trp Val Asp Ala Glu Leu Gly Ser Asp Ile 145 150 160 Tyr Leu Asp Gly Ile Ile Thr Ile Val Asp Ser Lys Tyr Gly Leu Lys His Leu Thr Glu Glu Lys Pro Asp Gly Leu Ile Asn Glu Ala Thr Arg 180 185 Gln Val Ala Leu Ala Asp Ala Ile Leu Ile Asn Lys Thr Asp Leu Val Pro Glu Glu Asp Val Lys Lys Leu Arg Thr Thr Ile Arg Ser Ile Asn Gly Leu Gly Gln Ile Leu Glu Thr Gln Arg Ser Arg Val Asp Leu Ser 225 230 235 Asn Val Leu Asp Leu His Ala Phe Asp Ser Leu Ser Gly Ile Ser Leu 255 250 255 Gln Lys Lys Leu Gln His Val Pro Gly Thr Gln Pro His Leu Asp Gln 260 265 270 Ser Ile Val Thr Ile Thr Phe Glu Val Pro Gly Asn Ala Lys Glu Glu 275 280 285 His Leu Asn Met Phe Ile Gln Asn Leu Leu Trp Glu Lys Asn Val Arg 290 300 Asn Lys Asp Asn His Cys Met Glu Val Ile Arg Leu Lys Gly Leu Val 305 $$310\$ Ser Ile Lys Asp Lys Ser Gln Gln Val Ile Val Gln Gly Val His Glu 325 330 335 Leu Tyr Asp Leu Glu Glu Thr Pro Val Ser Trp Lys Asp Asp Thr Glu 340 345 Arg Thr Asn Arg Leu Val Leu Leu Gly Arg Asn Leu Asp Lys Asp Ile 355 360 365 Leu Lys Gln Leu Phe Ile Ala Thr Val Thr Glu Thr Glu Lys Gln Trp 370 375 380

Thr Thr Arg Phe Gln Glu Asp Gln Val Cys Thr 385 390 395

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<400> 73

Met Glu Ala Glu Arg Arg Pro Ala Pro Gly Ser Pro Ser Glu Gly Leu 15

Phe Ala Asp Gly His Leu Ile Leu Trp Thr Leu Cys Ser Val Leu Leu 25

Pro Val Phe Ile Thr Phe Trp Cys Ser Leu Gln Arg Ser Arg Arg Gln 45

Leu His Arg Arg Asp Ile Phe Arg Lys Ser Lys His Gly Trp Arg Asp 55

<210> 73 <211> 567

<212> PRT <213> Homo sapiens

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Asp Leu Phe Ser Gln Pro Thr Tyr Cys Cys Val Cys Ala Gln His Ile Leu Gln Gly Ala Phe Cys Asp Cys Cys Gly Leu Arg Val Asp Glu Gly Cys Leu Arg Lys Ala Asp Lys Arg Phe Gln Cys Lys Glu Ile Met Leu Lys Asn Asp Thr Lys Val Leu Asp Ala Met Pro His His Trp Ile 115 120 125 Arg Gly Asn Val Pro Leu Cys Ser Tyr Cys Met Val Cys Lys Gln Gln
130 135 140 Cys Gly Cys Gln Pro Lys Leu Cys Asp Tyr Arg Cys Ile Trp Cys Gln 145 150 160 Lys Thr Val His Asp Glu Cys Met Lys Asn Ser Leu Lys Asn Glu Lys 165 170 175 Cys Asp Phe Gly Glu Phe Lys Asn Leu Ile Ile Pro Pro Ser Tyr Leu $180 \hspace{0.25cm} 185 \hspace{0.25cm} 190 \hspace{0.25cm}$ Thr Ser Ile Asn Gln Met Arg Lys Asp Lys Lys Thr Asp Tyr Glu Val 195 200 205 Leu Ala Ser Lys Leu Gly Lys Gln Trp Thr Pro Leu Ile Ile Leu Ala 210 215 220 Asn Ser Arg Ser Gly Thr Asn Met Gly Glu Gly Leu Leu Gly Glu Phe Arg Ile Leu Leu Asn Pro Val Gln Val Phe Asp Val Thr Lys Thr Pro Pro Ile Lys Ala Leu Gln Leu Cys Thr Leu Leu Pro Tyr Tyr Ser Ala 260 265 270 Arg Val Leu Val Cys Gly Gly Asp Gly Thr Val Gly Trp Val Leu Asp 275 280 285 Ala val Asp Asp Met Lys Ile Lys Gly Gln Glu Lys Tyr Ile Pro Gln 290 300 Val Ala Val Leu Pro Leu Gly Thr Gly Asn Asp Leu Ser Asn Thr Leu Gly Trp Gly Thr Gly Tyr Ala Gly Glu Ile Pro Val Ala Gln Val Leu 325 330 335 Arg Asn Val Met Glu Ala Asp Gly Ile Lys Leu Asp Arg Trp Lys Val 340 350 Gln val Thr Asn Lys Gly Tyr Tyr Asn Leu Arg Lys Pro Lys Glu Phe 355 360 365 Thr Met Asn Asn Tyr Phe Ser Val Gly Pro Asp Ala Leu Met Ala Leu 370 380 Asn Phe His Ala His Arg Glu Lys Ala Pro Ser Leu Phe Ser Ser Arg

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ile Leu Asn Lys Ala Val Tyr Leu Phe Tyr Gly Thr Lys Asp Cys Leu
405 410 415

Val Gln Glu Cys Lys Asp Leu Asn Lys Lys Val Glu Leu Glu Leu Asp 420 425 430 Gly Glu Arg Val Ala Leu Pro Ser Leu Glu Gly Ile Ile Val Leu Asn 445 445 Ile Gly Tyr Trp Gly Gly Gly Cys Arg Leu Trp Glu Gly Met Gly Asp $450 \ \ 455 \ \ 460$ Glu Thr Tyr Pro Leu Ala Arg His Asp Asp Gly Leu Leu Glu Val Val 465 470 480 Gly Val Tyr Gly Ser Phe His Cys Ala Gln Ile Gln Val Lys Leu Ala 485 490 495 Asn Pro Phe Arg Ile Gly Gln Ala His Thr Val Arg Leu Ile Leu Lys
500 505 510 Cys Ser Met Met Pro Met Gln Val Asp Gly Glu Pro Trp Ala Gln Gly 515 525 Pro Cys Thr Val Thr Ile Thr His Lys Thr His Ala Met Met Leu Tyr 530 540 Phe Ser Gly Glu Gln Thr Asp Asp Asp Ile Ser Ser Thr Ser Asp Gln 545 550 560 Glu Asp Ile Lys Ala Thr Glu 565

74 542 PRT

Homo sapiens

Met Thr Lys Ser Asn Gly Glu Glu Pro Lys Met Gly Gly Arg Met Glu
1 10 15 Arg Phe Gln Gly Val Arg Lys Arg Thr Leu Leu Ala Lys Lys Lys Val Gln Asn Ile Thr Lys Glu Asp Val Lys Ser Tyr Leu Phe Arg Asn 35 40 45 Ala Phe Val Leu Leu Thr Val Thr Ala Val Ile Val Gly Thr Ile Leu 50 55 60 Gly Phe Thr Leu Arg Pro Tyr Arg Met Ser Tyr Arg Glu Val Lys Tyr 65 75 80 Phe Ser Phe Pro Gly Glu Leu Leu Met Arg Met Leu Gln Met Leu Val Leu pro Leu Ile Ile Ser Ser Leu Val Thr Gly Met Ala Ala Leu Asp $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$ Ser Lys Ala Ser Gly Lys Met Gly Met Arg Ala Val Val Tyr Tyr Met

Thr Thr Thr Ile Ile Ala Val Val Ile Gly Ile Ile Val Ile Ile 130 135 140

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile His Pro Gly Lys Gly Thr Lys Glu Asn Met His Arg Glu Gly Lys Ile Val Arg Val Thr Ala Ala Asp Ala Phe Leu Asp Leu Ile Arg Asn 165 170 175 Met Phe Pro Pro Asn Leu Val Glu Ala Cys Phe Lys Gln Phe Lys Thr 180 185 190 Asn Tyr Glu Lys Arg Ser Phe Lys Val Pro Ile Gln Ala Asn Glu Thr Leu Val Gly Ala Val Ile Asn Asn Val Ser Glu Ala Met Glu Thr Leu 210 215 220 Thr Arg Ile Thr Glu Glu Leu Val Pro Val Pro Gly Ser Val Asn Gly 225 230 240 Val Asn Ala Leu Gly Leu Val Val Phe Ser Met Cys Phe Gly Phe Val 245 250 255 Ile Gly Asn Met Lys Glu Gln Gly Gln Ala Leu Arg Glu Phe Phe Asp 260 270 Ser Leu Asn Glu Ala Ile Met Arg Leu Val Ala Val Ile Met Trp Tyr 275 280 285 Ala Pro Val Gly Ile Leu Phe Leu Ile Ala Gly Lys Ile Val Glu Met Glu Asp Met Gly Val Ile Gly Gly Gln Leu Ala Met Tyr Thr Val Thr 305 310 315 320 Val Ile Val Gly Leu Leu Ile His Ala Val Ile Val Leu Pro Leu Leu 325 330 335 Tyr Phe Leu Val Thr Arg Lys Asn Pro Trp Val Phe Ile Gly Gly Leu Leu Gln Ala Leu Ile Thr Ala Leu Gly Thr Ser Ser Ser Ser Ala Thr 355 360 365 Leu Pro Ile Thr Phe Lys Cys Leu Glu Glu Asn Asn Gly Val Asp Lys Arg Val Thr Arg Phe Val Leu Pro Val Gly Ala Thr Ile Asn Met Asp 385 390 395 400 Gly Thr Ala Leu Tyr Glu Ala Leu Ala Ala Ile Phe Ile Ala Gln Val 405 410 415 Asn Asn Phe Glu Leu Asn Phe Gly Gln Ile Ile Thr Ile Ser Ile Thr 420 425 430Ala Thr Ala Ala Ser Ile Gly Ala Ala Gly Ile Pro Gln Ala Gly Leu 435 440 445 Val Thr Met Val Ile Val Leu Thr Ser Val Gly Leu Pro Thr Asp Asp 450 460 Ile Thr Leu Ile Ile Ala Val Asp Trp Phe Leu Asp Arg Leu Arg Thr 465 470 475 480 Thr Thr Asn Val Leu Gly Asp Ser Leu Gly Ala Gly Ile Val Glu His

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Leu Ser Arg His Glu Leu Lys Asn Arg Asp Val Glu Met Gly Asn Ser 500 505

Val Ile Glu Glu Asn Glu Met Lys Lys Pro Tyr Gln Leu Ile Ala Gln 515 520 525

Asp Asn Glu Thr Glu Lys Pro Ile Asp Ser Glu Thr Lys Met 530 540

<210> 75 <211> 2647 <212> PRT <213> Homo sapiens

Met Ser Ser Ser His Ser Arg Ala Gly Gln Ser Ala Ala Gly Ala Ala 1 10 15

Pro Gly Gly Val Asp Thr Arg Asp Ala Glu Met Pro Ala Thr Glu

Lys Asp Leu Ala Glu Asp Ala Pro Trp Lys Lys Ile Gln Gln Asn Thr 35 40 45

Phe Thr Arg Trp Cys Asn Glu His Leu Lys Cys Val Ser Lys Arg Ile

Ala Asn Leu Gln Thr Asp Leu Ser Asp Gly Leu Arg Leu Ile Ala Leu 65 70 80

Leu Glu Val Leu Ser Gln Lys Lys Met His Arg Lys His Asn Gln Arg

Pro Thr Phe Arg Gln Met Gln Leu Glu Asn Val Ser Val Ala Leu Glu 100 105 110

Phe Leu Asp Arg Glu Ser Ile Lys Leu Val Ser Ile Asp Ser Lys Ala 115 120 125

Ile Leu His Tyr Ser Ile Ser Met Pro Met Trp Asp Glu Glu Glu Asp 145 150 150 160

Glu Glu Ala Lys Lys Gln Thr Pro Lys Gln Arg Leu Leu Gly Trp Ile 165 170 175

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Gin Ser Gly Arg Ala Leu Gly Ala Leu Val Asp Ser Cys Ala Pro Gly 195 200 205

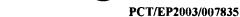
Leu Cys Pro Asp Trp Asp Ser Trp Asp Ala Ser Lys Pro Val Thr Asn

Ala Arg Glu Ala Met Gln Gln Ala Asp Asp Trp Leu Gly Ile Pro Gln 225 230 235 240

Val Ile Thr Pro Glu Glu Ile Val Asp Pro Asn Val Asp Glu His Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Val Met Thr Tyr Leu Ser Gln Phe Pro Lys Ala Lys Leu Lys Pro Gly
260 265 270

Ala Pro Leu Arg Pro Lys Leu Asn Pro Lys Lys Ala Arg Ala Tyr Gly
275 280 285 Pro Gly Ile Glu Pro Thr Gly Asn Met Val Lys Lys Arg Ala Glu Phe 290 295 300 Thr Val Glu Thr Arg Ser Ala Gly Gln Gly Glu Val Leu Val Tyr Val 305 310 315 320 Glu Asp Pro Ala Gly His Gln Glu Glu Ala Lys Val Thr Ala Asn Asn 335 Asp Lys Asn Arg Thr Phe Ser Val Trp Tyr Val Pro Glu Val Thr Gly 340 350 Thr His Lys Val Thr Val Leu Phe Ala Gly Gln His Ile Ala Lys Ser Pro Phe Glu Val Tyr Val Asp Lys Ser Gln Gly Asp Ala Ser Lys Val Thr Ala Gln Gly Pro Gly Leu Glu Pro Ser Gly Asn Ile Ala Asn Lys Thr Thr Tyr Phe Glu Ile Phe Thr Ala Gly Ala Gly Thr Gly Glu Val Glu Val Val Ile Gln Asp Pro Met Gly Gln Lys Gly Thr Val Glu Pro
420 425 430 Gln Leu Glu Ala Arg Gly Asp Ser Thr Tyr Arg Cys Ser Tyr Gln Pro Thr Met Glu Gly Val His Thr Val His Val Thr Phe Ala Gly Val Pro Ile Pro Arg Ser Pro Tyr Thr Val Thr Val Gly Gln Ala Cys Asn Pro
465 470 475 480 Ser Ala Cys Arg Ala Val Gly Arg Gly Leu Gln Pro Lys Gly Val Arg 485 490 495 Val Lys Glu Thr Ala Asp Phe Lys Val Tyr Thr Lys Gly Ala Gly Ser 500 505 Gly Glu Leu Lys Val Thr Val Lys Gly Pro Lys Gly Glu Glu Arg Val Lys Gln Lys Asp Leu Gly Asp Gly Val Tyr Gly Phe Glu Tyr Tyr Pro 530 Met val Pro Gly Thr Tyr Ile Val Thr Ile Thr Trp Gly Gly Gln Asn 545 550 555 560 Ile Gly Arg Ser Pro Phe Glu Val Lys Val Gly Thr Glu Cys Gly Asn 575 Gln Lys Val Arg Ala Trp Gly Pro Gly Leu Glu Gly Gly Val Val Gly
580 585 590 Lys Ser Ala Asp Phe Val Val Glu Ala Ile Gly Asp Asp Val Gly Thr



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Gly Phe Ser Val Glu Gly Pro Ser Gln Ala Lys Ile Glu Cys Asp 610 620 Asp Lys Gly Asp Gly Ser Cys Asp Val Arg Tyr Trp Pro Gln Glu Ala 625 630 635 640 Gly Glu Tyr Ala Val His Val Leu Cys Asn Ser Glu Asp Ile Arg Leu 645 650 655 Ser Pro Phe Met Ala Asp Ile Arg Asp Ala Pro Gln Asp Phe His Pro 660 670 Asp Arg Val Lys Ala Arg Gly Pro Gly Leu Glu Lys Thr Gly Val Ala 675 680 685 Val Asn Lys Pro Ala Glu Phe Thr Val Asp Ala Lys His Gly Gly Lys 690 695 700 Ala Pro Leu Arg Val Gln Val Gln Asp Asn Glu Gly Cys Pro Val Glu 705 710 720 Ala Leu Val Lys Asp Asn Gly Asn Gly Thr Tyr Ser Cys Ser Tyr Val 725 730 735 Pro Arg Lys Pro Val Lys His Thr Ala Met Val Ser Trp Gly Gly Val 740 745 750 Ser Ile Pro Asn Ser Pro Phe Arg Val Asn Val Gly Ala Gly Ser His 755 760 765 Pro Asn Lys Val Lys Val Tyr Gly Pro Gly Val Ala Lys Thr Gly Leu 770 780 Lys Ala His Glu Pro Thr Tyr Phe Thr Val Asp Cys Ala Glu Ala Gly 785 790 795 Gln Gly Asp Val Ser Ile Gly Ile Lys Cys Ala Pro Gly Val Val Gly 805 810 815 Pro Ala Glu Ala Asp Ile Asp Phe Asp Ile Ile Arg Asn Asp Asn Asp 820 825 830 Thr Phe Thr Val Lys Tyr Thr Pro Arg Gly Ala Gly Ser Tyr Thr Ile 835 840 845 Met Val Leu Phe Ala Asp Gln Ala Thr Pro Thr Ser Pro Ile Arg Val 850 855 860 Lys Val Glu Pro Ser His Asp Ala Ser Lys Val Lys Ala Glu Gly Pro 865 870 875 Gly Leu Ser Arg Thr Gly Val Glu Leu Gly Lys Pro Thr His Phe Thr 885 890 895 Val Asn Ala Lys Ala Ala Gly Lys Gly Lys Leu Asp Val Gln Phe Ser Gly Leu Thr Lys Gly Asp Ala Val Arg Asp Val Asp Ile Ile Asp His 915 920 925 His Asp Asn Thr Tyr Thr Val Lys Tyr Thr Pro Val Gln Gln Gly Pro

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Val Gly Val Asn Val Thr Tyr Gly Gly Asp Pro Ile Pro Lys Ser Pro
945 950 955 960

Phe Ser Val Ala Val Ser Pro Ser Leu Asp Leu Ser Lys Ile Lys Val 965 975

Ser Gly Leu Gly Glu Lys Val Asp Val Gly Lys Asp Gln Glu Phe Thr 980 985 990

Val Lys Ser Lys Gly Ala Gly Gly Gln Gly Lys Val Ala Ser Lys Ile 995 1000 1005

Val Gly Pro Ser Gly Ala Ala Val Pro Cys Lys Val Glu Pro Gly 1010 1015

Leu Gly Ala Asp Asn Ser Val Val Arg Phe Leu Pro Arg Glu Glu 1025 1030 1035

Gly Pro Tyr Glu Val Glu Val Thr Tyr Asp Gly Val Pro Val Pro 1040 1050

Gly Ser Pro Phe Pro Leu Glu Ala Val Ala Pro Thr Lys Pro Ser 1055 1060 1065

Lys Val Lys Ala Phe Gly Pro Gly Leu Gln Gly Gly Ser Ala Gly 1070 1080

Ser Pro Ala Arg Phe Thr Ile Asp Thr Lys Gly Ala Gly Thr Gly 1085 1090

Gly Leu Gly Leu Thr Val Glu Gly Pro Cys Glu Ala Gln Leu Glu 1100 11105 1110

Cys Leu Asp Asn Gly Asp Gly Thr Cys Ser Val Ser Tyr Val Pro 1115 1120 1125

Thr Glu Pro Gly Asp Tyr Asn Ile Asn Ile Leu Phe Ala Asp Thr 1130 1140

His Ile Pro Gly Ser Pro Phe Lys Ala His Val Val Pro Cys Phe 1145 1150

Asp Ala Ser Lys Val Lys Cys Ser Gly Pro Gly Leu Glu Arg Ala 1160 1165 1170

Thr Ala Gly Glu Val Gly Gln Phe Gln Val Asp Cys Ser Ser Ala 1175 1180

Gly Ser Ala Glu Leu Thr Ile Glu Ile Cys Ser Glu Ala Gly Leu 1190 1195 1200

Pro Ala Glu Val Tyr Ile Gln Asp His Gly Asp Gly Thr His Thr 1205 1210

Ile Thr Tyr Ile Pro Leu Cys Pro Gly Ala Tyr Thr Val Thr Ile 1220 1230

Lys Tyr Gly Gln Pro Val Pro Asn Phe Pro Ser Lys Leu Gln 1235 1240 1245

Val Glu Pro Ala Val Asp Thr Ser Gly Val Gln Cys Tyr Gly Pro 1250 1260

Gly Ile Glu Gly Gln Gly Val Phe Arg Glu Ala Thr Thr Glu Phe 1265 1270 1275

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Val Asp Ala Arg Ala Leu Thr Gln Thr Gly Gly Pro His Val 1280 1285 1290 Lys Ala Arg Val Ala Asn Pro Ser Gly Asn Leu Thr Glu Thr Tyr 1295 1300 1305 Val Gln Asp Arg Gly Asp Gly Met Tyr Lys Val Glu Tyr Thr Pro Tyr Glu Glu Gly Leu His Ser Val Asp Val Thr Tyr Asp Gly Ser 1325 1330 1335 Pro Val Pro Ser Ser Pro Phe Gln Val Pro Val Thr Glu Gly Cys 1340 1345 1350 Asp Pro Ser Arg Val Arg Val His Gly Pro Gly Ile Gln Ser Gly 1355 1360 1365 Thr Thr Asn Lys Pro Asn Lys Phe Thr Val Glu Thr Arg Gly Ala 1370 1380 Gly Thr Gly Gly Leu Gly Leu Ala Val Glu Gly Pro Ser Glu Ala Lys Met Ser Cys Met Asp Asn Lys Asp Gly Ser Cys Ser Val Glu 1400 1410 1410Tyr Ile Pro Tyr Glu Ala Gly Thr Tyr Ser Leu Asn Val Thr Tyr 1415 1420 1425 Gly Gly His Gln Val Pro Gly Ser Pro Phe Lys Val Pro Val His 1430 1440 Asp Val Thr Asp Ala Ser Lys Val Lys Cys Ser Gly Pro Gly Leu 1445 1450 1455 Ser Pro Gly Met Val Arg Ala Asn Leu Pro Gln Ser Phe Gln Val 1460 1465 1470 Asp Thr Ser Lys Ala Gly Val Ala Pro Leu Gln Val Lys Val Gln 1475 1480 1485 Gly Pro Lys Gly Leu Val Glu Pro Val Asp Val Val Asp Asn Ala 1490 1495 1500 Asp Gly Thr Gln Thr Val Asn Tyr Val Pro Ser Arg Glu Gly Pro 1505 1510 1515 Tyr Ser Ile Ser Val Leu Tyr Gly Asp Glu Glu Val Pro Arg Ser 1520 1530 Pro Phe Lys Val Lys Val Leu Pro Thr His Asp Ala Ser Lys Val 1535 1540 1545 Lys Ala Ser Gly Pro Gly Leu Asn Thr Thr Gly Val Pro Ala Ser Leu Pro Val Glu Phe Thr Ile Asp Ala Lys Asp Ala Gly Glu Gly 1565 1570 1575 Leu Leu Ala Val Gln Ile Thr Asp Pro Glu Gly Lys Pro Lys Lys

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr His Ile Gln Asp Asn His Asp Gly Thr Tyr Thr Val Ala Tyr 1595 1600 1605

Val Pro Asp Val Thr Gly Arg Tyr Thr Ile Leu Ile Lys Tyr Gly 1610 1620

Gly Asp Glu Ile Pro Phe Ser Pro Tyr Arg Val Arg Ala Val Pro 1625 1635

Thr Gly Asp Ala Ser Lys Cys Thr Val Thr Val Ser Ile Gly Gly 1640 1650

His Gly Leu Gly Ala Gly Ile Gly Pro Thr Ile Gln Ile Gly Glu 1655 1660 1665

Glu Thr Val Ile Thr Val Asp Thr Lys Ala Ala Gly Lys Gly Lys 1670 1680

Val Thr Cys Thr Val Cys Thr Pro Asp Gly Ser Glu Val Asp Val 1685 1690 1695

Asp Val Val Glu Asn Glu Asp Gly Thr Phe Asp Ile Phe Tyr Thr

Ala Pro Gln Pro Gly Lys Tyr Val Ile Cys Val Arg Phe Gly Gly 1715 1720 1725

Glu His Val Pro Asn Ser Pro Phe Gln Val Thr Ala Leu Ala Gly 1730 1740

Asp Gln Pro Ser Val Gln Pro Pro Leu Arg Ser Gln Gln Leu Ala

Pro Gln Tyr Thr Tyr Ala Gln Gly Gly Gln Gln Thr Trp Ala Pro 1760 1770

Glu Arg Pro Leu Val Gly Val Asn Gly Leu Asp Val Thr Ser Leu 1775 1780 1785

Arg Pro Phe Asp Leu Val Ile Pro Phe Thr Ile Lys Lys Gly Glu

Ile Thr Gly Glu Val Arg Met Pro Ser Gly Lys Val Ala Gln Pro 1805 Val 1810

Thr Ile Thr Asp Asn Lys Asp Gly Thr Val Thr Val Arg Tyr Ala 1820 1825 1830

Pro Ser Glu Ala Gly Leu His Glu Met Asp Ile Arg Tyr Asp Asn 1835 1840 1845

Met His Ile Pro Gly Ser Pro Leu Gln Phe Tyr Val Asp Tyr Val 1850 1860

ASN CYS Gly His Val Thr Ala Tyr Gly Pro Gly Leu Thr His Gly 1865 1870 1875

Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn Thr Lys Asp Ala 1880 1885 1890

Gly Glu Gly Gly Leu Ser Leu Ala Ile Glu Gly Pro Ser Lys Ala 1895 1900 1905

Glu Ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys Ser Val Ser

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Tyr Leu Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Val Lys Tyr 1925 1930 1935 Asn Glu Gln His Val Pro Gly Ser Pro Phe Thr Ala Arg Val Thr 1940 1950 Gly Asp Asp Ser Met Arg Met Ser His Leu Lys Val Gly Ser Ala 1955 1960 1965 Ala Asp Ile Pro Ile Asn Ile Ser Glu Thr Asp Leu Ser Leu Leu 1970 1980 Thr Ala Thr Val Val Pro Pro Ser Gly Arg Glu Glu Pro Cys Leu 1985 1990 1995 Leu Lys Arg Leu Arg Asn Gly His Val Gly Ile Ser Phe Val Pro 2000 2005 2010 Lys Glu Thr Gly Glu His Leu Val His Val Lys Lys Asn Gly Gln 2015 2020 2025 His Val Ala Ser Ser Pro Ile Pro Val Val Ile Ser Gln Ser Glu 2030 2035 2040 Ile Gly Asp Ala Ser Arg Val Arg Val Ser Gly Gln Gly Leu His 2045 2050 2055 Glu Gly His Thr Phe Glu Pro Ala Glu Phe Ile Ile Asp Thr Arg 2060 2065 2070 Asp Ala Gly Tyr Gly Gly Leu Ser Leu Ser Ile Glu Gly Pro Ser 2075 2080 2085 Lys Val Asp Ile Asn Thr Glu Asp Leu Glu Asp Gly Thr Cys Arg 2090 2100 Val Thr Tyr Cys Pro Thr Glu Pro Gly Asn Tyr Ile Ile Asn Ile 2105 2110 2115 Lys Phe Ala Asp Gln His Val Pro Gly Ser Pro Phe Ser Val Lys 2120 2125 2130 Val Thr Gly Glu Gly Arg Val Lys Glu Ser Ile Thr Arg Arg Arg 2135 2140 2145 Arg Ala Pro Ser Val Ala Asn Val Gly Ser His Cys Asp Leu Ser Leu Lys Ile Pro Glu Ile Ser Ile Gln Asp Met Thr Ala Gln Val 2165 2170 2175 Thr Ser Pro Ser Gly Lys Thr His Glu Ala Glu Ile Val Glu Gly 2180 2185 2190 Glu Asn His Thr Tyr Cys Ile Arg Phe Val Pro Ala Glu Met Gly 2195 2200 2205 Thr His Thr Val Ser Val Lys Tyr Lys Gly Gln His Val Pro Gly Ser pro Phe Gln Phe Thr Val Gly Pro Leu Gly Glu Gly Gly Ala 2225 2230 2235

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Lys Val Arg Ala Gly Gly Pro Gly Leu Glu Arg Ala Glu Ala 2240 2245 2250

Gly Val Pro Ala Glu Phe Ser Ile Trp Thr Arg Glu Ala Gly Ala 2255 2260 2265

Gly Gly Leu Ala Ile Ala Val Glu Gly Pro Ser Lys Ala Glu Ile 2270 2280

Ser Phe Glu Asp Arg Lys Asp Gly Ser Cys Gly Val Ala Tyr Val 2285 2290 2295

Val Gln Glu Pro Gly Asp Tyr Glu Val Ser Val Lys Phe Asn Glu 2300 2305 2310

Glu His Ile Pro Asp Ser Pro Phe Val Val Pro Val Ala Ser Pro 2315 2320 2325

Ser Gly Asp Ala Arg Arg Leu Thr Val Ser Ser Leu Gln Glu Ser 2330 2335 2340

Gly Leu Lys Val Asn Gln Pro Ala Ser Phe Ala Val Ser Leu Asn 2345 2350 2355

Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Pro Ser Gly 2360 2370

Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr

Ala Val Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu Ile Asp 2390 2395 2400

Val Lys Phe Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys Ile $2405\,$ 2415

Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser 2420 2430

Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala 2435 2440 2445

Glu Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser 2450 2460

Val Thr Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu 2465 \cdot 2475

Cys Pro Glu Gly Tyr Arg Val Thr Tyr Thr Pro Met Ala Pro Gly

Ser Tyr Leu Ile Ser Ile Lys Tyr Gly Gly Pro Tyr His Ile Gly
2495 2500 2505

Gly Ser Pro Phe Lys Ala Lys Val Thr Gly Pro Arg Leu Val Ser

Asn His Ser Leu His Glu Thr Ser Ser Val Phe Val Asp Ser Leu 2525 2530 2535

Thr Lys Ala Thr Cys Ala Pro Gln His Gly Ala Pro Gly Pro Gly

Pro Ala Asp Ala Ser Lys Val Val Ala Lys Gly Leu Gly Leu Ser 2555 2560 2565 Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Lys Ala Tyr Val Gly Gln Lys Ser Ser Phe Thr Val Asp Cys Ser

Lys Ala Gly Asn Asn Met Leu Leu Val Gly Val His Gly Pro Arg 2585 2590 2595

Thr Pro Cys Glu Glu Ile Leu Val Lys His Val Gly Ser Arg Leu 2600 2610

Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu Tyr Thr Leu 2615 2625

Val Val Lys Trp Gly His Glu His Ile Pro Gly Ser Pro Tyr Arg 2630 2640

val Val Val Pro 2645

<210> 76 <211> 395 <212> PRT -213> Homo sapiens

Met Ala Val Thr Asp Ser Leu Ser Arg Ala Ala Thr Val Leu Ala Thr

Val Leu Leu Ser Phe Gly Ser Val Ala Ala Ser His Ile Glu Asp 20 30

Gln Ala Glu Gln Phe Phe Arg Ser Gly His Thr Asn Asn Trp Ala Val $35 ext{ } 40 ext{ } 45$

Leu Val Cys Thr Ser Arg Phe Trp Phe Asn Tyr Arg His Val Ala Asn 50 60

Thr Leu Ser Val Tyr Arg Ser Val Lys Arg Leu Gly Ile Pro Asp Ser 65 70 75 80

His Ile Val Leu Met Leu Ala Asp Asp Met Ala Cys Asn Pro Arg Asn 90 95

Pro Lys Pro Ala Thr Val Phe Ser His Lys Asn Met Glu Leu Asn Val

Tyr Gly Asp Asp Val Glu Val Asp Tyr Arg Ser Tyr Glu Val Thr Val 115 120 125

Glu Asn Phe Leu Arg Val Leu Thr Gly Arg Ile Pro Pro Ser Thr Pro 130 140

Arg Ser Lys Arg Leu Leu Ser Asp Asp Arg Ser Asn Ile Leu Ile Tyr 145 150 155 160

Met Thr Gly His Gly Gly Asn Gly Phe Leu Lys Phe Gln Asp Ser Glu 175 175

Glu Ile Thr Asn Ile Glu Leu Ala Asp Ala Phe Glu Gln Met Trp Gln 180 185 190

Lys Arg Arg Tyr Asn Glu Leu Leu Phe Ile Ile Asp Thr Cys Gln Gly 195 200 205

Ala ser Met Tyr Glu Arg Phe Tyr Ser Pro Asn Ile Met Ala Leu Ala

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Ser Gln Val Gly Glu Asp Ser Leu Ser His Gln Pro Asp Pro Ala 225 230 235 240 Ile Gly Val His Leu Met Asp Arg Tyr Thr Phe Tyr Val Leu Glu Phe Leu Glu Glu Ile Asn Pro Ala Ser Gln Thr Asn Met Asn Asp Leu Phe 260 265 270 Gln Val Cys Pro Lys Ser Leu Cys Val Ser Thr Pro Gly His Arg Thr Asp Leu Phe Gln Arg Asp Pro Lys Asn Val Leu Ile Thr Asp Phe Phe 290 295 300 Gly Ser Val Arg Lys Val Glu Ile Thr Thr Glu Thr Ile Lys Leu Gln 305 310 315 320 Gln Asp Ser Glu Ile Met Glu Ser Ser Tyr Lys Glu Asp Gln Met Asp Glu Lys Leu Met Glu Pro Leu Lys Tyr Ala Glu Gln Leu Pro Val Ala 340 345 350 Gln Ile Ile His Gln Lys Pro Lys Leu Lys Asp Trp His Pro Pro Gly 355 360 365 Gly Phe Ile Leu Gly Leu Trp Ala Leu Ile Ile Met Val Phe Phe Lys $370 \hspace{1cm} 375 \hspace{1cm} 380$ Thr Tyr Gly Ile Lys His Met Lys Phe Ile Phe 385 390

Met Glu Ala Ile Ala Lys Tyr Asp Phe Lys Ala Thr Ala Asp Asp Glu 1 5 10 Leu Ser Phe Lys Arg Gly Asp Ile Leu Lys Val Leu Asn Glu Glu Cys Asp Gln Asn Trp Tyr Lys Ala Glu Leu Asn Gly Lys Asp Gly Phe Ile 35 40 45 Pro Lys Asn Tyr Ile Glu Met Lys Pro His Pro Trp Phe Phe Gly Lys 50 55 60 Ile Pro Arg Ala Lys Ala Glu Glu Met Leu Ser Lys Gln Arg His Asp 65 70 75 80 Gly Ala Phe Leu Ile Arg Glu Ser Glu Ser Ala Pro Gly Asp Phe Ser Leu Ser Val Lys Phe Gly Asn Asp Val Gln His Phe Lys Val Leu Arg 100 105 110 Asp Gly Ala Gly Lys Tyr Phe Leu Trp Val Val Lys Phe Asn Ser Leu 115 120 125

<210> 77 <211> 217 <212> PRT <213> Homo sapiens

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.sT25.txt
Asn Glu Leu Val Asp Tyr His Arg Ser Thr Ser Val Ser Arg Asn Gln
130
135

Gln Ile Phe Leu Arg Asp Ile Glu Gln Val Pro Gln Gln Pro Thr Tyr 145

Val Gln Ala Leu Phe Asp Phe Asp Pro Gln Glu Asp Gly Glu Leu Gly Phe Arg Arg Gly Asp Phe Ile His Val Met Asp Asn Ser Asp Pro Asn 185

Trp Trp Lys Gly Ala Cys His Gly Gln Thr Gly Met Phe Pro Arg Asn Tyr Val Thr Pro Val Asn Arg Asn Val

<210> 78 <211> 443

<213> Homo sapiens

<400> 78

Met Glu Cys Leu Arg Ser Leu Pro Cys Leu Leu Pro Arg Ala Met Arg Leu Pro Arg Arg Thr Leu Cys Ala Leu Ala Leu Asp Val Thr Ser Val Gly Pro Pro Val Ala Ala Cys Gly Arg Arg Ala Asn Leu Ile Gly Arg Ser Arg Ala Ala Gln Leu Cys Gly Pro Asp Arg Leu Arg Val Ala Gly Glu Val His Arg Phe Arg Thr Ser Asp Val Ser Gln Ala Thr Leu Ala 65 70 75 80 Ser Val Ala Pro Val Phe Thr Val Thr Lys Phe Asp Lys Gln Gly Asn 95 Val Thr Ser Phe Glu Arg Lys Lys Thr Glu Leu Tyr Gln Glu Leu Gly
100 105 110 Leu Gln Ala Arg Asp Leu Arg Phe Gln His Val Met Ser Ile Thr Val Arg Asn Asn Arg Ile Ile Met Arg Met Glu Tyr Leu Lys Ala Val Ile 130 140 Thr Pro Glu Cys Leu Leu Ile Leu Asp Tyr Arg Asn Leu Asn Leu Glu 145 150 160 Gin Trp Leu Phe Arg Glu Leu Pro Ser Gin Leu Ser Gly Glu Gly Gin 165 170 175 Leu Val Thr Tyr Pro Leu Pro Phe Glu Phe Arg Ala Ile Glu Ala Leu 180 185 Leu Gln Tyr Trp Ile Asn Thr Leu Gln Gly Lys Leu Ser Ile Leu Gln 195 200 205 Pro Leu Ile Leu Glu Thr Leu Asp Ala Leu Val Asp Pro Lys His Ser

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protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Val Asp Arg Ser Lys Leu His Ile Leu Leu Gln Asn Gly Lys Ser Leu Ser Glu Leu Glu Thr Asp Ile Lys Ile Phe Lys Glu Ser Ile Leu 245 250 250 Glu Ile Leu Asp Glu Glu Glu Leu Leu Glu Glu Leu Cys Val Ser Lys 260 265 270 Trp Ser Asp Pro Gln Val Phe Glu Lys Ser Ser Ala Gly Ile Asp His Ala Glu Glu Met Glu Leu Leu Glu Asn Tyr Tyr Arg Leu Ala Asp 290 295 300 Asp Leu Ser Asn Ala Ala Arg Glu Leu Arg Val Leu Ile Asp Asp Ser 305 310315 Gln Ser Ile Ile Phe Ile Asn Leu Asp Ser His Arg Asn Val Met Met 325 330 335 Arg Leu Asn Leu Gin Leu Thr Met Gly Thr Phe Ser Leu Ser Leu Phe Gly Leu Met Gly Val Ala Phe Gly Met Asn Leu Glu Ser Ser Leu Glu 355 360 365 Glu Asp His Arg Ile Phe Trp Leu Île Thr Gly Ile Met Phe Met Gly Ser Gly Leu Ile Trp Arg Arg Leu Leu Ser Phe Leu Gly Arg Gln Leu 385 390 395 400 Glu Ala Pro Leu Pro Pro Met Met Ala Ser Leu Pro Lys Lys Thr Leu 405 410 415 Leu Ala Asp Arg Ser Met Glu Leu Lys Asn Ser Leu Arg Leu Asp Gly
420 425 430 Leu Gly Ser Gly Arg Ser Ile Leu Thr Asn Arg

<210> 79 <211> 1928

<212> PRT <213> Homo sapiens

<400> 79

Gly Gln Val Arg Arg Arg Leu Gln Glu Leu Asp Gly Glu Leu Glu Ala la Ala Leu Gly Leu Leu Asp Ile Ile Leu Ala Lys Asn Pro Ser Gly Leu Thr Gln Tyr Ile Pro Val Leu Val Asp Ser Phe Leu Pro Leu Leu Lys 45

Ser pro Leu Ala Ala Pro Arg Ile Lys Asn Pro Phe Leu Ser Leu Ala

Ala cys Val Met Pro Ser Arg Leu Lys Ala Leu Gly Thr Leu Val Ser

His val Thr Leu Arg Leu Leu Lys Pro Glu Cys Val Leu Asp Lys Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Trp Cys Gln Glu Leu Ser Val Ala Val Lys Arg Ala Val Met Leu
100 105 110 Leu His Thr His Thr Ile Thr Ser Arg Val Gly Lys Gly Glu Pro Gly
115 120 125 Ala Ala Pro Leu Ser Ala Pro Ala Phe Ser Leu Val Phe Pro Phe Leu 130 135 140 Lys Met Val Leu Thr Glu Met Pro His His Ser Glu Glu Glu Glu Glu 145 150 155 160 Trp Met Ala Gln Ile Leu Gln Ile Leu Thr Val Gln Ala Gln Leu Arg 165 170 175 Ala Ser Pro Asn Thr Pro Pro Gly Arg Val Asp Glu Asn Gly Pro Glu 180 185 190 Leu Leu Pro Arg Val Ala Met Leu Arg Leu Leu Thr Trp Val Ile Gly 195 200 205 Thr Gly Ser Pro Arg Leu Gln Val Leu Ala Ser Asp Thr Leu Thr Thr 210 215 220 Leu Cys Ala Ser Ser Ser Gly Asp Asp Gly Cys Ala Phe Ala Glu Gln 225 230 235 Glu Glu Val Asp Val Leu Leu Cys Ala Leu Gln Ser Pro Cys Ala Ser 245 250 255 Val Arg Glu Thr Val Leu Arg Gly Leu Met Glu Leu His Met Val Leu 260 265 270 Pro Ala Pro Asp Thr Asp Glu Lys Asn Gly Leu Asn Leu Leu Arg Arg 275 280 285 Leu Trp Val Val Lys Phe Asp Lys Glu Glu Glu Ile Arg Lys Leu Ala Glu Arg Leu Trp Ser Met Met Gly Leu Asp Leu Gln Pro Asp Leu Cys 305 310 315 Ser Leu Leu Ile Asp Asp Val Ile Tyr His Glu Ala Ala Val Arg Gln Ala Gly Ala Glu Ala Leu Ser Gln Ala Val Ala Arg Tyr Gln Arg Gln
340 345 350 Ala Ala Glu Val Met Gly Arg Leu Met Glu Ile Tyr Gln Glu Lys Leu 355 360 365 Tyr Arg Pro Pro Pro Val Leu Asp Ala Leu Gly Arg Val Ile Ser Glu Ser Pro Pro Asp Gln Trp Glu Ala Arg Cys Gly Leu Ala Leu Ala Leu 385 390 395 400 Asn Lys Leu Ser Gln Tyr Leu Asp Ser Ser Gln Val Lys Pro Leu Phe 405 410 415

Gln Phe Phe Val Pro Asp Ala Leu Asn Asp Arg His Pro Asp Val Arg 420 425 430

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Lys Cys Met Leu Asp Ala Ala Leu Ala Thr Leu Asn Thr His Gly Lys
435
440
445

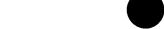
Glu Asn Val Asn Ser Leu Leu Pro Val Phe Glu Glu Phe Leu Lys Asn 450 455 460 Ala Pro Asn Asp Ala Ser Tyr Asp Ala Val Arg Gln Ser Val Val 480 465 470 475 Leu Met Gly Ser Leu Ala Lys His Leu Asp Lys Ser Asp Pro Lys Val Lys Pro Ile Val Ala Lys Leu Ile Ala Ala Leu Ser Thr Pro Ser Gln 505 Gln Val Gln Glu Ser Val Ala Ser Cys Leu Pro Pro Leu Val Pro Ala 515 520 525 Ile Lys Glu Asp Ala Gly Gly Met Ile Gln Arg Leu Met Gln Gln Leu 530 540 Leu Glu Ser Asp Lys Tyr Ala Glu Arg Lys Gly Ala Ala Tyr Gly Leu 545 550 560 Ala Gly Leu Val Lys Gly Leu Gly Ile Leu Ser Leu Lys Gln Gln Glu 575 Met Met Ala Ala Leu Thr Asp Ala Ile Gln Asp Lys Lys Asn Phe Arg 580 585 Arg Arg Glu Gly Ala Leu Phe Ala Phe Glu Met Leu Cys Thr Met Leu 595 600 605 Gly Lys Leu Phe Glu Pro Tyr Val Val His Val Leu Pro His Leu Leu 610 615 620 Leu Cys Phe Gly Asp Gly Asn Gln Tyr Val Arg Glu Ala Ala Asp Asp 625 636 Cys Ala Lys Ala Val Met Ser Asn Leu Ser Ala His Gly Val Lys Leu 645 650 655 Val Leu Pro Ser Leu Leu Ala Ala Leu Glu Glu Glu Ser Trp Arg Thr 660 665 670 Lys Ala Gly Ser Val Glu Leu Leu Gly Ala Met Ala Tyr Cys Ala Pro 675 680 685 Lys Gln Leu Ser Ser Cys Leu Pro Asn Ile Val Pro Lys Leu Thr Glu Val Leu Thr Asp Ser His Val Lys Val Gln Lys Ala Gly Gln Gln Ala
705 710 715 720 Leu Arg Gln Ile Gly Ser Val Ile Arg Asn Pro Glu Ile Leu Ala Ile 725 730 735 Ala Pro Val Leu Leu Asp Val Leu Thr Asp Pro Ser Arg Lys Thr Gln 745 750 Lys Cys Leu Gln Thr Leu Leu Asp Thr Lys Phe Val His Phe Ile Asp 760 765 Ala Pro Ser Leu Ala Leu Ile Met Pro Ile Val Gln Arg Ala Phe Gln 770 780

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asp Arg Ser Thr Asp Thr Arg Lys Met Ala Ala Gln Ile Ile Gly Asn 785 790 795 Met Tyr Ser Leu Thr Asp Gln Lys Asp Leu Ala Pro Tyr Leu Pro Ser 805 810 815 Val Thr Pro Gly Leu Lys Ala Ser Leu Leu Asp Pro Val Pro Glu Val 820 825 830 Arg Thr val Ser Ala Lys Ala Leu Gly Val Met Val Lys Gly Met Gly 835 840 845 Glu Ser Cys Phe Glu Asp Leu Leu Pro Trp Leu Met Glu Thr Leu Thr 850 860 Tyr Glu Gln Ser Ser Val Asp Arg Ser Gly Ala Ala Gln Gly Leu Ala 865 870 875 Glu Val Met Ala Gly Leu Gly Val Glu Lys Leu Glu Lys Leu Met Pro Glu Ile Val Ala Thr Ala Ser Lys Val Asp Ile Ala Pro His Val Arg 900 905 910 Asp Gly Tyr Ile Met Met Phe Asn Tyr Leu Pro Ile Thr Phe Gly Asp Lys Phe Thr Pro Tyr Val Gly Pro Ile Ile Pro Cys Ile Leu Lys Ala 930 940 Leu Ala Asp Glu Asn Glu Phe Val Arg Asp Thr Ala Leu Arg Ala Gly 945 950 955 960 Gln Arg Val Ile Ser Met Tyr Ala Glu Thr Ala Ile Ala Leu Leu Leu 965 970 975 Pro Gln Leu Glu Gln Gly Leu Phe Asp Asp Leu Trp Arg Ile Arg Phe 980 985 990 Ser Ser Val Gln Leu Leu Gly Asp Leu Leu Phe His Ile Ser Gly Val 995 1000 1005 Thr Gly Lys Met Thr Thr Glu Thr Ala Ser Glu Asp Asp Asn Phe 1010 1020 Gly Thr Ala Gln Ser Asn Lys Ala Ile Ile Thr Ala Leu Gly Val 1025 1030 1035 Glu Arg Arg Asn Arg Val Leu Ala Gly Leu Tyr Met Gly Arg Ser 1040 1050 Asp Thr Gln Leu Val Val Arg Gln Ala Ser Leu His Val Trp Lys 1055 1060 1065 Ile Val Val Ser Asn Thr Pro Arg Thr Leu Arg Glu Ile Leu Pro 1070 1080 Thr Leu Phe Gly Leu Leu Gly Phe Leu Ala Ser Thr Cys Ala 1085 1090 1095 Asp Lys Arg Thr Ile Ala Ala Arg Thr Leu Gly Asp Leu Val Arg 1100 1110 1110

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Lys Leu Gly Glu Lys Ile Leu Pro Glu Ile Ile Pro Ile Leu Glu
1115 1120 1125

Glu Gly Leu Arg Ser Gln Lys Ser Asp Glu Arg Gln Gly Val Cys 1130 1140 Ile Gly Leu Ser Glu Ile Met Lys Ser Thr Ser Arg Asp Ala Val 1145 1155 Leu Tyr Phe Ser Glu Ser Leu Val Pro Thr Ala Arg Lys Ala Leu 1160 1170 Cys Asp Pro Leu Glu Glu Val Arg Glu Ala Ala Lys Thr Phe Glu Gln Leu His Ser Thr Ile Gly His Gln Ala Leu Glu Asp Ile 1190 1200 Leu Pro Phe Leu Leu Lys Gln Leu Asp Asp Glu Glu Val Ser Glu Phe Ala Leu Asp Gly Leu Lys Gln Val Met Ala Ile Lys Ser Arg Val Val Leu Pro Tyr Leu Val Pro Lys Leu Thr Thr Pro Pro Val 1235 1240 1245 Asn Thr Arg Val Leu Ala Phe Leu Ser Ser Val Ala Gly Asp Ala 1250 1260 Leu Thr Arg His Leu Gly Val Ile Leu Pro Ala Val Met Leu Ala Leu Lys Glu Lys Leu Gly Thr Pro Asp Glu Gln Leu Glu Met Ala 1280 1285 1290 Asn Cys Gln Ala Val Ile Leu Ser Val Glu Asp Asp Thr Gly His 1295 1300 1305 Arg Ile Ile Glu Asp Leu Leu Glu Ala Thr Arg Ser Pro Glu val Gly Met Arg Gln Ala Ala Ala Ile Ile Leu Asn Ile Tyr Cys 1325 1330 1335 Ser Arg Ser Lys Ala Asp Tyr Thr Ser His Leu Arg Ser Leu Val 1340 1345 1350 Ser Gly Leu Ile Arg Leu Phe Asn Asp Ser Ser Pro Val Val Leu 1355 1360 1365 Glu Glu Ser Trp Asp Ala Leu Asp Ala Ile Thr Lys Lys Leu Asp Ala Gly Asn Gln Leu Ala Leu Ile Glu Glu Leu His Lys Glu Ile 1385 1390 1395 Arg Leu Ile Gly Asn Glu Ser Lys Gly Glu His Val Pro Gly Phe 1400 1405 1410 Cys Leu Pro Lys Lys Gly Val Thr Ser Ile Leu Pro Val Leu Arg 1415 1420 1425 Glu Gly Val Leu Thr Gly Ser Pro Glu Gln Lys Glu Glu Ala Ala 1430 1435 1440



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Lys Ala Leu Gly Leu Val Ile Arg Leu Thr Ser Ala Asp Val Leu 1445 1450 1455 Arg Pro Ser Val Val Ser Ile Thr Gly Pro Leu Ile Arg Ile Leu 1460 1470 Gly Asp arg Phe Ser Trp Asn Val Lys Ala Ala Leu Leu Glu Thr 1475 1480 1485 Leu Ser Leu Leu Leu Ala Lys Val Gly Ile Ala Leu Lys Pro Phe 1490 1500 Leu Pro Gln Leu Gln Thr Thr Phe Thr Lys Ala Leu Gln Asp Ser 1505 1510 1515 Asn Arg Gly Val Arg Leu Lys Ala Ala Asp Ala Leu Gly Lys Leu 1520 1530 Ile Ser Ile His Ile Lys Val Asp Pro Leu Phe Thr Glu Leu Leu 1535 1540 1545 Asn Gly Ile Arg Ala Met Glu Asp Pro Gly Val Arg Asp Thr Met Leu Gln Ala Leu Arg Phe Val Ile Gln Gly Ala Gly Ala Lys Val Asp Ala Val Ile Arg Lys Asn Ile Val Ser Leu Leu Ser Met 1580 1585 1590 Leu Gly His Asp Glu Asp Asn Thr Arg Ile Ser Ser Ala Gly Cys Leu Gly Glu Leu Cys Ala Phe Leu Thr Glu Glu Glu Leu Ser Ala 1610 1620 Val Leu Gln Gln Cys Leu Leu Ala Asp Val Ser Gly Ile Asp Trp 1625 1630 1635 Met Val Arg His Gly Arg Ser Leu Ala Leu Ser Val Ala Val Asn 1640 1645 1650 Val Ala Pro Gly Arg Leu Cys Ala Gly Arg Tyr Ser Ser Asp Val 1655 1660 1665 Gln Glu Met Ile Leu Ser Ser Ala Thr Ala Asp Arg Ile Pro Ile 1670 1680 Ala val Ser Gly Val Arg Gly Met Gly Phe Leu Met Arg His His 1685 1690 1695 Ile Glu Thr Gly Gly Gly Gln Leu Pro Arg Lys Leu Ser Ser Leu 1700 1705 1710 Phe val Lys Cys Leu Gln Asn Pro Ser Ser Asp Ile Arg Leu Val Ala Glu Lys Met Ile Trp Trp Ala Asn Lys Asp Pro Leu Pro Pro Leu Asp Pro Gln Ala Ile Lys Pro Ile Leu Lys Ala Leu Leu Asp

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Asn Thr Lys Asp Lys Asn Thr Val Val Arg Ala Tyr Ser Asp Gln
1760 1765 1770

Ala Ile Val Asn Leu Leu Lys Met Arg Gln Gly Glu Glu Val Phe

Gln Ser Leu Ser Lys Ile Leu Asp Val Ala Ser Leu Glu Val Leu 1790 1800

Asn Glu Val Asn Arg Arg Ser Leu Lys Lys Leu Ala Lys Pro Gly 1805 1815

Arg Leu His Gly Ala Gly Gly Arg His His Pro Asp Met Arg Gly 1820 1830

Leu Gly Ser Ser Ser Ile Ala Ala Pro His Leu Cys Ser Met Phe 1835 1840 1845

Ser Phe Leu Lys Ile His Leu Phe Gln Trp Gly Ala Trp Lys Met 1850 1860

Ala Phe Pro Glu Ser Ile Leu Ile Ser Ile Asp His Ser Gln Ser 1870 1875

Leu Lys Ser Asn Pro His Thr Thr Glu Asn Cys Leu Leu His Leu 1880 1885 1890

Ser Pro Phe Pro Val Glu Lys Arg Arg Lys Ser Thr Arg Met Arg 1895 1900 1905

Leu Ser Lys Trp Gln Pro Arg Ser Cys Leu Ser Ser Leu Ala Trp 1910 1915 1920

Leu Gly Leu Glu Leu 1925

<210> 80 <211> 325 <212> PRT

Homo sapiens

<400> 80

Met Ala Leu Ala Asp Ser Thr Arg Gly Leu Pro Asn Gly Gly Gly Gly 10 15

Gly Gly Ser Gly Ser Ser Ser Ser Ser Ala Glu Pro Pro Leu Phe $20 \ \ 25 \ \ 30$

Pro Asp Ile Val Glu Leu Asn Val Gly Gly Gln Val Tyr Val Thr Arg

arg cys Thr Val Val Ser Val Pro Asp Ser Leu Leu Trp Arg Met Phe 50 60

Thr Gln Gln Gln Pro Gln Glu Leu Ala Arg Asp Ser Lys Gly Arg Phe 65 70 75 80

Phe Leu ASP Arg Asp Gly Phe Leu Phe Arg Tyr Ile Leu Asp Tyr Leu 85 90 95

Arg Asp Leu Gln Leu Val Leu Pro Asp Tyr Phe Pro Glu Arg Ser Arg $100 \ 105 \ \mathrm{Li}$

Leu Gln Arg Glu Ala Glu Tyr Phe Glu Leu Pro Glu Leu Val Arg Arg 115 120 125

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Gly Ala Pro Gln Gln Pro Gly Pro Gly Pro Pro Pro Ser Arg Arg 130 135 140

Gly Val His Lys Glu Gly Ser Leu Gly Asp Glu Leu Leu Pro Leu Gly 145 150 160 Tyr Ser Glu Pro Glu Gln Gln Glu Gly Ala Ser Ala Gly Ala Pro Ser 165 170 175 Pro Thr Leu Glu Leu Ala Ser Arg Ser Pro Ser Gly Gly Ala Ala Gly 180 185 190 Pro Leu Leu Thr Pro Ser Gln Ser Leu Asp Gly Ser Arg Arg Ser Gly Tyr Ile Thr Ile Gly Tyr Arg Gly Ser Tyr Thr Ile Gly Arg Asp Ala Gln Ala Asp Ala Lys Phe Arg Arg Val Ala Arg Ile Thr Val Cys Gly 225 230 240 Lys Thr Ser Leu Ala Lys Glu Val Phe Gly Asp Thr Leu Asn Glu Ser 245 250 255 Arg Asp Pro Asp Arg Pro Pro Glu Arg Tyr Thr Ser Arg Tyr Tyr Leu Lys Phe Asn Phe Leu Glu Gln Ala Phe Asp Lys Leu Ser Glu Ser Gly 275 280 285 Phe His Met Val Ala Cys Ser Ser Thr Gly Thr Cys Ala Phe Ala Ser 290 300 Ser Thr Asp Gln Ser Glu Asp Lys Ile Trp Thr Ser Tyr Thr Glu Tyr 305 310 315 320val Phe Cys Arg Glu

<210> <211> <212> <213>

Homo sapiens

<400> 81

Met Arg Arg Asp Val Arg Ile Leu Leu Gly Glu Ala Gln Val Gly 1 10 15 Lys Thr Ser Leu Ile Leu Ser Leu Val Gly Glu Glu Phe Pro Glu Glu 20 25 Val Pro Pro Arg Ala Glu Glu Ile Thr Ile Pro Ala Asp Val Thr Pro 35 40 45 Glu Lys Val Pro Thr His Ile Val Asp Tyr Ser Glu Ala Glu Gln Thr 50 60Asp Glu Glu Leu Arg Glu Glu Ile His Lys Ala Asn Val Val Cys Val val Tyr Asp val Ser Glu Glu Ala Thr Ile Glu Lys Ile Arg Thr Lys

Trp Ile Pro Leu Val Asn Gly Gly Thr Thr Gln Gly Pro Arg Val Pro



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Ile Leu Val Gly Asn Lys Ser Asp Leu Arg Ser Gly Ser Ser Met Glu Ala Val Leu Pro Ile Met Ser Gln Phe Pro Glu Ile Glu Thr Cys 130 135 140 Val Glu Cys Ser Ala Lys Asn Leu Arg Asn Ile Ser Glu Leu Phe Tyr 145 150 160 Tyr Ala Gln Lys Ala Val Leu His Pro Thr Ala Pro Leu Tyr Asp Pro 165 170 175 Glu Ala Lys Gln Leu Arg Pro Ala Cys Ala Gln Ala Leu Thr Arg Ile 180 185 190 Phe Arg Leu Ser Asp Gln Asp Leu Asp Gln Ala Leu Ser Asp Glu Glu
195 200 205 Leu Asn Ala Phe Gln Lys Ser Cys Phe Gly His Pro Leu Ala Pro Gln 210 220 Ala Leu Glu Asp Val Lys Thr Val Val Cys Arg Asn Val Ala Gly Gly 225 230 240 Val Arg Glu Asp Arg Leu Thr Leu Asp Gly Phe Leu Phe Leu Asn Thr Leu Phe Ile Gln Arg Gly Arg His Glu Thr Thr Trp Thr Ile Leu Arg $260 \hspace{1.5cm} 265 \hspace{1.5cm} 270 \hspace{1.5cm}$ Arg Phe Gly Tyr Ser Asp Ala Leu Glu Leu Thr Ala Asp Tyr Leu Ser 275 280 285 Pro Leu Ile His Val Pro Pro Gly Cys Ser Thr Glu Leu Asn His Leu 290 295 300 Gly Tyr Gln Phe Val Gln Arg Val Phe Glu Lys His Asp Gln Asp Arg 305 310 315 320 Asp Gly Ala Leu Ser Pro Val Glu Leu Gln Ser Leu Phe Ser Val Phe 325 330 335 Pro Ala Ala Pro Trp Gly Pro Glu Leu Pro Arg Thr Val Arg Thr Glu 340 345 350 Ala Gly Arg Leu Pro Leu His Gly Tyr Leu Cys Gln Trp Thr Leu Val Thr Tyr Leu Asp Val Arg Ser Cys Leu Gly His Leu Gly Tyr Leu Gly 370 380 Tyr Pro Thr Leu Cys Glu Gln Asp Gln Ala His Ala Ile Thr Val Thr 385 390 395 400 Arg Glu Lys Arg Leu Asp Gln Glu Lys Gly Gln Thr Gln Arg Ser Val 405 410 415 Leu Leu Cys Lys Val Val Gly Ala Arg Gly Val Gly Lys Ser Ala Phe Leu Gln Ala Phe Leu Gly Arg Gly Leu Gly His Gln Asp Thr Arg Glu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Gln Pro Pro Gly Tyr Ala Ile Asp Thr Val Gln Val Asn Gly Gln Glu
450
455
460

Lys Tyr Leu Ile Leu Cys Glu Val Gly Thr Asp Gly Leu Leu Ala Thr 465 470 475 480

Ser Leu Asp Ala Thr Cys Asp Val Ala Cys Leu Met Phe Asp Gly Ser 485 490 495

Asp Pro Lys Ser Phe Ala His Cys Ala Ser Val Tyr Lys His His Tyr $500 \hspace{1.5cm} 505 \hspace{1.5cm} 510$

Met Asp Gly Gln Thr Pro Cys Leu Phe Val Ser Ser Lys Ala Asp Leu
515 520 525

Pro Glu Gly Val Ala Val Ser Gly Pro Ser Pro Ala Glu Phe Cys Arg 530 540

Lys His Arg Leu Pro Ala Pro Val Pro Phe Ser Cys Ala Gly Pro Ala 545 550 555 560

Glu Pro Ser Thr Thr Ile Phe Thr Gln Leu Ala Thr Met Ala Ala Phe

Pro His Leu Val His Ala Glu Leu His Pro Ser Ser Phe Trp Leu Arg

Gly Leu Leu Gly Val Val Gly Ala Ala Val Ala Ala Val Leu Ser Phe

Ser Leu Tyr Arg Val Leu Val Lys Ser Gln 610

<210> 82 <211> 69 <212> PRT <213> Homo sapiens

<400> 82

Val Met Leu Ala Ala Ser Tyr Trp Ser Leu Leu Ala Pro Ala Val Glu 1 10 15

Met Ala Thr Ser Ser Gly Gly Phe Gly Ala Phe Ala Phe Pro Val

Ala Val Gly Phe Thr Leu Gly Ala Ala Phe Val Tyr Leu Ala Asp Leu 35 40 45

Leu Met Pro His Leu Lys Asn Cys Pro Leu Asp Gln Thr Ala Glu Cys
50 55 60

Asp Val Gly Arg Leu

<210> 83 <211> 731 <212> PRT <213> Homo sapiens

Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu Val 1 5 10

Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile 20 25 30

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile
35 40 45

Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Thr Leu Thr 50 60Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu Ile 65 70 75 80 Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile Gly
85 90 95 Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser 100 105 110 Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser 115 120 125 Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala 130 140Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala 145 150 155 160 Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys Lys 195 200 205 His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys Glu 210 215 220 Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp Lys Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro Glu 245 250 255 Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Lys Lys Asp Gly Asp 265 270 Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln Glu Glu 275 280 285 Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp Ile Thr ASN Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp Trp Glu 305 310 315 320 ASP His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu Glu Phe 325 330 335 Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu Phe Glu Asn Arg Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Asn Cys Glu Glu Leu Ile Pro Glu Tyr Leu Asn Phe Ile Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser Arg Glu 385 390 400 Met Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn Leu Val 405 410 415Lys Lys Cys Leu Glu Leu Phe Thr Glu Leu Ala Glu Asp Lys Glu Asn 420 430 Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu Gly Ile 435 440 445His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu Arg Tyr 450 460 Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp Tyr Cys 465 470 475 Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Tyr Ile Thr Gly Glu 485 490 495 Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu Arg Lys 500 505 His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu Tyr Cys 515 525 val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser Val Thr 530 535 540 Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Lys Lys Lys Gln 545 550 555 Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met Lys Asp 565 570 575 Ile Leu Glu Lys Lys Val Glu Lys Val Val Ser Asn Arg Leu Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala Asn $595 \hspace{1.5cm} 600 \hspace{1.5cm} 605$ Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr Met 610 615 620 Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp His Ser 625 630 635 640 Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp Lys 655 655 Ser val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu Leu Ser 660 670Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg Ile Tyr 675 680 685 Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro Thr Ala 690 700 Asp Asp Thr Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu Glu Gly 705 710 715 720

Protein Complexes of cellular metworks underlying the development of cancer and other diseases.ST25.txt
Asp Asp Asp Thr Ser Arg Met Glu Glu Val-Asp
730

<210> 84

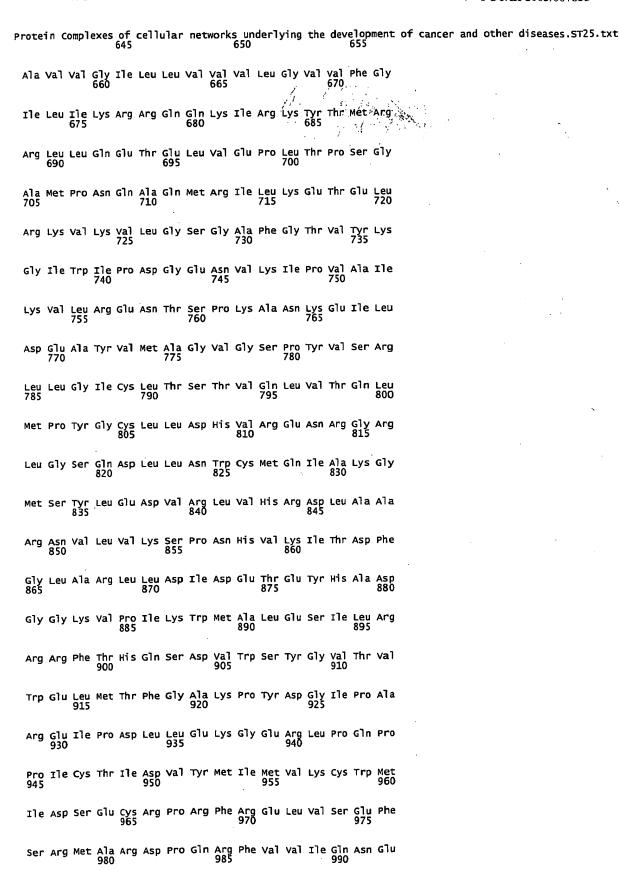
<212> PRT

213> Homo sapiens

<400> Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu $10 \ 15$ Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys $\frac{20}{30}$ Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val 65 70 75 80 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu 85 90 95 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr 100 105 110 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro 115 120 125 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser 130 135 140 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln 145 150 160 Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser 195 200 205 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys 210 220 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys 225 230 235 240 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu 245 250 255 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val 260 265 270 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg 275 280 285

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln 305 310 315 320 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys 325 330 335 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu 345 350 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys 355 360 365 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro $405 \hspace{0.25cm} 410 \hspace{0.25cm} 415$ Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg 420 420 430 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly 450 455 460 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val 465 470 475 480 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr 485 490 495 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His 500 505 510 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys 515 520 525 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys 530 540 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys 545 550 555 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565 570 575 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp 585 590 Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu 595 605 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser





Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
995 1000 1005

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr 1010 1020

Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly 1025 1030 1035

Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg

Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu 1055 1060 1065

Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser 1070 1080

Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu 1085 1090 1095

Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser 1100 1110 1110

Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val

Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro 1130 1140

Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro Leu Pro 1145 1150 1155

Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro Lys Thr Leu 1160 1165 1170

Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly 1175 1180 1185

Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln Gly Gly Ala 1190 1200

Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala Phe Asp 1205 1210 1215

ASN Leu Tyr Tyr Trp ASP Gln ASP Pro Pro Glu Arg Gly Ala Pro 1220 1230

Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr 1235 1240 1245

Leu Gly Leu Asp Val Pro Val 1250 1255

<210> 85 <211> 296 <212> PRT

<212> PKI <213> Homo sapiens

~400× 85

Ala Glu Gly Met Val Cys Asn His Leu Cys Ser Ser Asp Gly Cys Trp 10 15

Gly Pro Gly Pro Asp Gln Cys Leu Ser Cys Arg Arg Phe Ser Arg Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Ile Cys Ile Glu Ser Cys Asn Leu Tyr Asp Gly Gly Asn Asp Thr 35 40 45 Thr Phe Leu Phe Ser Phe Phe Phe Val Phe Thr Phe Gln Gly Pro Asp 50 60 Asn Cys Thr Lys Cys Ser His Phe Lys Asp Gly Pro Asn Cys Val Glu 65 70 75 80 Lys Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser Phe Ile Phe Lys Tyr $90 \hspace{0.5in} 95$ Ala Asp Pro Asp Arg Glu Cys His Pro Cys His Pro Asn Cys Thr Gln $100 \ \ 105 \ \ \ 110$ Gly Thr Pro Leu Ile Ala Ala Gly Val Ile Gly Gly Leu Phe Ile Leu Val Ile Val Gly Leu Thr Phe Ala Val Tyr Val Arg Arg Lys Ser Ile 130 140 Lys Lys Lys Arg Ala Leu Arg Arg Phe Leu Glu Thr Glu Leu Val Glu 145 150 160 Pro Leu Thr Pro Ser Gly Thr Ala Pro Asn Gln Ala Gln Leu Arg Ile 165 170 175 Leu Lys Glu Thr Glu Leu Lys Arg Val Lys Val Leu Gly Ser Gly Ala 180 185 Phe Gly Thr Val Tyr Lys Gly Ile Trp Val Pro Glu Gly Glu Thr Val 195 200 205 Lys Ile Pro Val Ala Ile Lys Ile Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met Asp 225 230 240 His Pro His Leu Val Arg Leu Leu Gly Val Cys Leu Ser Pro Thr Ile 245 250 255 Gln Leu Val Thr Gln Leu Met Pro His Gly Cys Leu Leu Glu Tyr Val 260 265 270 His Glu His Lys Asp Asn Ile Gly Ser Gln Leu Leu Asn Trp Cys 280 285 val Gln Ile Ala Lys Val Ser Ala 290 295

<210> 86 <211> 1257 <212> PRT <213> Homo sapiens

<400>

Met Ala Ser Cys Ser Phe Thr Arg Asp Gln Ala Thr Arg Arg Leu Arg 1 10 15 Gly Ala Ala Ala Ala Ala Ala Leu Ala Ala Val Val Thr Thr 20 25 30

Pro Leu Leu Ser Ser Gly Thr Pro Thr Ala Leu Ile Gly Thr Gly Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Cys Pro Gly Ala Met Trp Leu Ser Thr Ala Thr Gly Ser Arg Ser Asp Ser Glu Ser Glu Glu Glu Asp Leu Pro Val Gly Glu Glu Val Cys 65 75 80 Lys Arg Gly Tyr Leu Arg Lys Gln Lys His Gly His Arg Arg Tyr Phe 85 90 95 Val Leu Lys Leu Glu Thr Ala Asp Ala Pro Ala Arg Leu Glu Tyr Tyr 100 105 110 Glu Asn Ala Arg Lys Phe Arg His Ser Val Arg Ala Ala Ala Ala Ala 115 120 125 Ala Ala Ala Ala Ser Gly Ala Ala Ile Pro Pro Leu Ile Pro Pro Arg Arg Val Ile Thr Leu Tyr Gln Cys Phe Ser Val Ser Gln Arg Ala Asp Ala Arg Tyr Arg His Leu Ile Ala Leu Phe Thr Gln Asp Glu Tyr 165 170 175 Phe Ala Met Val Ala Glu Asn Glu Ser Glu Gln Glu Ser Trp Tyr Leu 180 185 190 Leu Leu Ser Arg Leu Ile Leu Glu Ser Lys Arg Arg Cys Gly Thr 195 200 205 Leu Gly Ala Gln Pro Asp Gly Glu Pro Ala Ala Leu Ala Ala Ala Ala 210 220 Ala Ala Glu Pro Pro Phe Tyr Lys Asp Val Trp Gln Val Ile Val Lys 225 230 235 240 Pro Arg Gly Leu Gly His Arg Lys Glu Leu Ser Gly Val Phe Arg Leu 245 250 255 Cys Leu Thr Asp Glu Glu Val Val Phe Val Arg Leu Asn Thr Glu Val 260 265 270 Ala Ser val val Val Gln Leu Leu Ser Ile Arg Arg Cys Gly His Ser 275 280 285 Glu Gln Tyr Phe Phe Leu Glu Val Gly Arg Ser Thr Val Ile Gly Pro $290 \ \ 295 \ \ 300$ Gly Glu Leu Trp Met Gln Val Asp Asp Cys Val Val Ala Gln Asn Met 305 310 315 320 His Glu Leu Phe Leu Glu Lys Met Arg Ala Leu Cys Ala Asp Glu Tyr 325 330 335 Arg Ala Arg Cys Arg Ser Tyr Ser Ile Ser Ile Gly Ala His Leu Leu 340 350 Thr Leu Leu Ser Ala Arg Arg His Leu Gly Leu Val Pro Leu Glu Pro 355 360 Gly Gly Trp Leu Arg Arg Ser Arg Phe Glu Gln Phe Cys His Leu Arg 370 380

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ala Ile Gly Asp Gly Glu Asp Glu Met Leu Phe Thr Arg Arg Phe Val
385 400

Thr Pro Ser Glu Pro Val Ala His Ser Arg Arg Gly Arg Leu His Leu 405 410 415 Pro Arg Gly Arg Arg Ser Arg Arg Ala Val Ser Val Pro Ala Ser Phe 420 430 Phe Arg Arg Leu Ala Pro Ser Pro Ala Arg Pro Arg His Pro Ala Glu 435 440 445 Ala Pro Asn Asn Gly Ala Arg Leu Ser Ser Glu Val Ser Gly Ser Gly Ser Gly Asn Phe Gly Glu Glu Gly Asn Pro Gln Gly Lys Glu Asp Gln 465 470 475 480 Glu Gly Ser Gly Gly Asp Tyr Met Pro Met Asn Asn Trp Gly Ser Gly 485 490 495 Asn Gly Arg Gly Ser Gly Gly Gly Gly Ser Asn Gly Gln Gly Ser 500 505 510 Ser Ser His Ser Ser Gly Gly Asn Gln Cys Ser Gly Glu Gly Gln Gly 515 520 525 Ser Arg Gly Gly Gln Gly Ser Asn Gly Gln Gly Ser Gly Gly Asn Gln 530 540 Cys Ser Arg Asp Gly Gln Gly Thr Ala Gly Gly His Gly Ser Gly Gly 545 $\,$ 550 $\,$ 555 $\,$ Gly Gln Arg Pro Gly Gly Gly His Gly Ser Gly Gly Gly Gln Gly Pro 565 570 575 Gly Asp Gly His Gly Ser Gly Gly Gly Lys Asn Ser Gly Gly Gly Lys
580 585 590 Gly Ser Gly Ser Gly Lys Gly Ser Asp Gly Asp Glu Arg Gly Lys 595 600 Ser Leu Lys Lys Arg Ser Tyr Phe Gly Lys Leu Thr Gln Ser Lys Gln $610 \ \ \, 615 \ \ \, 620 \ \ \,$ Gly Gly Thr Gly Gly Lys Gly Lys Ser Gly Gly Arg Phe Arg Leu Tyr
645 650 655 Phe Cys Val Asp Arg Gly Ala Thr Lys Glu Cys Lys Glu Ala Lys Glu 665 670 Val Lys Asp Ala Glu Ile Pro Glu Gly Ala Ala Arg Gly Pro His Arg 675 680 685 Ala Arg Ala Phe Asp Glu Asp Glu Asp Pro Tyr Val Pro Met Arg Pro Gly Val Ala Thr Pro Leu Val Ser Ser Ser Asp Tyr Met Pro Met 705 710 720 Ala pro Gln Asn Val Ser Ala Ser Lys Lys Arg His Ser Arg Ser Pro

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 725 730 735 Phe Glu Asp Ser Arg Gly Tyr Met Met Met Phe Pro Arg Val Ser Pro 740 745 750Pro Pro Ala Pro Ser Pro Pro Lys Ala Pro Asp Thr Asn Lys Glu Asp 755 760 765 Asp Ser Lys Asp Asn Asp Ser Glu Ser Asp Tyr Met Phe Met Ala Pro Gly Ala Gly Ala Ile Pro Lys Asn Pro Arg Asn Pro Gln Gly Gly Ser 785 790 795 Ser Ser Lys Ser Trp Ser Ser Tyr Phe Ser Leu Pro Asn Pro Phe Arg 815 Ser Ser Pro Leu Gly Gln Asn Asp Asn Ser Glu Tyr Val Pro Met Leu 820 825 Pro Gly Lys Phe Leu Gly Arg Gly Leu Asp Lys Glu Val Ser Tyr Asn 835 840 845 Trp Asp Pro Lys Asp Ala Ala Ser Lys Pro Ser Gly Glu Gly Ser Phe 850 860 Ser Lys Pro Gly Asp Gly Gly Ser Pro Ser Lys Pro Ser Asp His Glu 865 870 880 Pro Pro Lys Asn Lys Ala Lys Arg Pro Asn Arg Leu Ser Phe Ile Thr 885 . 890 895 Lys Gly Tyr Lys Ile Lys Pro Lys Pro Gln Lys Pro Thr His Glu Gln 900 905 910 Arg Glu Ala Asp Ser Ser Ser Asp Tyr Val Asm Met Asp Phe Thr Lys 915 925 Arg Glu Ser Asn Thr Pro Ala Pro Ser Thr Gln Gly Leu Pro Asp Ser 930 940 Trp Gly Ile Ile Ala Glu Pro Arg Gln Ser Ala Phe Ser Asn Tyr Val 945 950 955 960 Asn val Glu Phe Gly Val Pro Phe Pro Asn Pro Ala Asn Asp Leu Ser ASP Leu Leu Arg Ala Ile Pro Arg Ala Asn Pro Leu Ser Leu Asp Ser 980 985 990 Ala Arg Trp Pro Leu Pro Pro Leu Pro Leu Ser Ala Thr Gly Ser Asn 995 1000 1005 Ala Ile Glu Glu Glu Gly Asp Tyr Ile Glu Val Ile Phe Asn Ser 1010 1015 1020 Ala Met Thr Pro Ala Met Ala Leu Ala Asp Ser Ala Ile Arg Tyr 1025 1030 1035 Asp Ala Glu Thr Gly Arg Ile Tyr Val Val Asp Pro Phe Ser Glu Cys Cys Met Asp Ile Ser Leu Ser Pro Ser Arg Cys Ser Glu Pro

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Pro Pro Val Ala Arg Leu Leu Gln Glu Glu Glu Gln Glu Arg Arg 1070 1080

Arg Pro Gln Ser Arg Ser Gln Ser Phe Phe Ala Ala Ala Arg Ala 1085 1090 Ala Val Ser Ala Phe Pro Thr Asp Ser Leu Glu Arg Asp Leu Ser 1100 11105 Pro Ser Ser Ala Pro Ala Val Ala Ser Ala Ala Glu Pro Thr Leu Ala Leu Ser Gln Val Val Ala Ala Ala Ser Ala Leu Ala Ala Ala 1130 1140 Pro Gly Ile Gly Ala Ala Ala Ala Ala Gly Phe Asp Ser Ala 1145 1150 1155 Ser Ala Arg Trp Phe Gln Pro Val Ala Asn Ala Ala Asp Ala Glu 1160 1165 1170

Ala Val Arg Gly Ala Gln Asp Val Ala Gly Gly Ser Asn Pro Gly 1175 1180 1185

Ala His Asn Pro Ser Ala Asn Leu Ala Arg Gly Asp Asn Gln Ala

Gly Gly Ala Ala Ala Ala Ala Ala Pro Glu Pro Pro Pro Arg

Ser Arg Arg Val Pro Arg Pro Pro Glu Arg Glu Asp Ser Asp Asn 1220 1230

Asp Asp Asp Thr His Val Arg Met Asp Phe Ala Arg Arg Asp Asn 1245

Gln Phe Asp Ser Pro Lys Arg Gly Arg 1250 1255

<210> 87 <211> 1111 <212> PRT <213> Homo sapiens

Ser Ser Leu Leu Glu Lys Met Thr Ser Ser Asp Lys Asp Phe Arg Phe 10 15

Met Ala Thr Ser Asp Leu Met Ser Glu Leu Gln Lys Asp Ser Ile Gln

Leu Asp Glu Asp Ser Glu Arg Lys Val Val Lys Met Leu Leu Arg Leu 40 45

Leu Glu Asp Lys Asn Gly Glu Val Gln Asn Leu Ala Val Lys Trp Leu 50 60

Gly val Pro Leu Gly Ala Phe His Ala Ser Leu Leu His Cys Leu Leu 65 70 75 80

Pro Gln Leu Ser Ser Pro Arg Leu Ala Val Arg Lys Arg Ala Val Gly

Ala Leu Gly His Leu Ala Thr Ala Cys Ser Thr Asp Leu Phe Val Glu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Ala Asp His Leu Leu Asp Arg Leu Pro Gly Pro Arg Val Pro Thr 115 120 125 Ser Pro Thr Ala Ile Arg Thr Leu Ile Gln Cys Leu Gly Ser Val Gly 130 140 Arg Gln Ala Gly His Arg Leu Gly Ala His Leu Asp Arg Leu Val Pro 145 150 160 Leu Val Glu Asp Phe Cys Asn Leu Asp Asp Glu Leu Arg Glu Ser 165 170 175 Cys Leu Gln Ala Phe Glu Ala Phe Leu Arg Lys Cys Pro Lys Glu Met 180 185 190 Gly Pro His Val Pro Asn Val Thr Ser Leu Cys Leu Gln Tyr Ile Lys 195 200 205 His Asp Pro Asn Tyr Asn Tyr Asp Ser Asp Glu Asp Glu Glu Gln Met Glu Thr Glu Asp Ser Glu Phe Ser Glu Gln Glu Ser Glu Asp Glu Tyr 225 230 235 240 Ser Asp Asp Asp Met Ser Trp Lys Val Arg Arg Ala Ala Ala Lys 245 250 255 Cys Ile Ala Ala Leu Ile Ser Ser Arg Pro Asp Leu Leu Pro Asp Phe $260 \hspace{1cm} 265 \hspace{1cm} 265 \hspace{1cm}$ His Cys Thr Leu Ala Pro Val Leu Ile Arg Arg Phe Lys Glu Arg Glu 275 280 285 Glu Asn Val Lys Ala Asp Val Phe Thr Ala Tyr Ile Val Leu Leu Arg Gln Thr Arg Pro Pro Lys Gly Trp Leu Glu Ala Met Glu Glu Pro Thr 305 310 315 320 Gln Thr Gly Ser Asn Leu His Met Leu Arg Gly Gln Val Pro Leu Val Val Lys Ala Leu Gln Arg Gln Leu Lys Asp Arg Ser Val Arg Ala Arg 340 345 350 Gln Gly Cys Phe Ser Leu Leu Thr Glu Leu Ala Gly Val Leu Pro Gly Ser Leu Ala Glu His Met Pro Val Leu Val Ser Gly Ile Ile Phe Ser 370 380 Leu Ala Asp Arg Ser Ser Ser Thr Ile Arg Met Asp Ala Leu Ala 385 390 395 400 Phe Leu Gln Gly Leu Leu Gly Thr Glu Pro Ala Glu Ala Phe His Pro 405 410 415 His Leu Pro Ile Leu Leu Pro Pro Val Met Ala Cys Val Ala Asp Ser 420 425 430 Phe Tyr Lys Ile Ala Ala Glu Ala Leu Val Val Leu Gln Glu Leu Val

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Arg Ala Leu Trp Pro Leu His Arg Pro Arg Met Leu Asp Pro Glu Pro
450
455
460

Tyr Val Gly Glu Met Ser Ala Val Thr Leu Ala Arg Leu Arg Ala Thr 465 470470475 Asp Leu Asp Gln Glu Val Lys Glu Arg Ala Ile Ser Cys Met Gly His 485 490 495 Leu Val Gly His Leu Gly Asp Arg Leu Gly Asp Asp Leu Glu Pro Thr 500 505 510 Leu Leu Leu Leu Asp Arg Leu Arg Asn Glu Ile Thr Arg Leu Pro 515 520 525 Ala Ile Lys Ala Leu Thr Leu Val Ala Val Ser Pro Leu Gln Leu Asp 530 540 Leu Gln Pro Ile Leu Ala Glu Ala Leu His Ile Leu Ala Ser Phe Leu 545 550 560 Arg Lys Asn Gln Arg Ala Leu Arg Leu Ala Thr Leu Ala Ala Leu Asp 570 575 Ala Leu Ala Gln Ser Gln Gly Leu Ser Leu Pro Pro Ser Ala Val Gln 585 590 Ala Val Leu Ala Glu Leu Pro Ala Leu Val Asn Glu Ser Asp Met His 595 600 605 Val Ala Gln Leu Ala Val Asp Phe Leu Ala Thr Val Thr Gln Ala Gln
610 620 Pro Ala Ser Leu Val Glu Val Ser Gly Pro Val Leu Ser Glu Leu Leu 625 630 635 640 Arg Leu Leu Arg Ser Pro Leu Leu Pro Ala Gly Val Leu Ala Ala Ala 650 655 Glu Gly Phe Leu Gln Ala Leu Val Gly Thr Arg Pro Pro Cys Val Asp 660 665 670 Tyr Ala Lys Leu Ile Ser Leu Leu Thr Ala Pro Val Tyr Glu Gln Ala 675 680 685 Val Asp Gly Gly Pro Gly Leu His Lys Gln Val Phe His Ser Leu Ala 690 695 700 Arg Cys Val Ala Ala Leu Ser Ala Ala Cys Pro Gln Glu Ala Ala Ser 705 710 715 720 Thr Ala Ser Arg Leu Val Cys Asp Ala Arg Ser Pro His Ser Ser Thr 725 730 735 Gly Val Lys Val Leu Ala Phe Leu Ser Leu Ala Glu Val Gly Gln Val 740 745 Ala Gly Pro Gly Pro Gln Arg Glu Leu Lys Ala Val Leu Leu Glu Ala 755 760 765 Leu Gly Ser Pro Ser Glu Asp Val Arg Ala Ala Ala Ser Tyr Ala Leu 770 780 Gly Arg Val Gly Ala Gly Ser Leu Pro Asp Phe Leu Pro Phe Leu Leu 785 790 795 800

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Gln Ile Glu Ala Glu Pro Arg Arg Gln Tyr Leu Leu Leu His Ser 805 810 815 Leu Arg Glu Ala Leu Gly Ala Ala Gln Pro Asp Ser Leu Lys Pro Tyr 820 825 830 Ala Glu Asp Ile Trp Ala Leu Leu Phe Gln Arg Cys Glu Gly Ala Glu 835 840 845 Glu Gly Thr Arg Gly Val Val Ala Glu Cys Ile Gly Lys Leu Val Leu 850 855 860 Val Asn Pro Ser Phe Leu Leu Pro Arg Leu Arg Lys Gln Leu Ala Ala 865 870 875 Gly Arg Pro His Thr Arg Ser Thr Val Ile Thr Ala Val Lys Phe Leu 885 890 895 Ile Ser Asp Gln Pro His Pro Ile Asp Pro Leu Leu Lys Ser Phe Ile $900 \hspace{1cm} 905 \hspace{1cm} 910$ Ala Val His Asn Lys Pro Ser Leu Val Arg Asp Leu Leu Asp Asp Ile 915 920 925 Leu Pro Leu Leu Tyr Gln Glu Thr Lys Ile Arg Arg Asp Leu Ile Arg 930 935 940Glu Val Glu Met Gly Pro Phe Lys His Thr Val Asp Asp Gly Leu Asp 945 950 960 Val Arg Lys Ala Ala Phe Glu Cys Met Tyr Ser Leu Leu Glu Ser Cys 965 970 975 Leu Gly Gln Leu Asp Ile Cys Glu Phe Leu Asn His Val Glu Asp Gly 985 985 Leu Lys Asp His Tyr Asp Ile Arg Met Leu Thr Phe Ile Met Val Ala 995 1000 1005 Arg Leu Ala Thr Leu Cys Pro Ala Pro Val Leu Gln Arg Val Asp 1010 1015 1020 Arg Leu Ile Glu Pro Leu Arg Ala Thr Cys Thr Ala Lys Val Lys 1025 1030 1035 Ala Gly Ser Val Lys Gln Glu Phe Glu Lys Gln Asp Glu Leu Lys 1040 1045 1050 Arg Ser Ala Met Arg Ala Val Ala Ala Leu Leu Thr Ile Pro Glu 1055 1060 1065Val Gly Lys Ser Pro Ile Met Ala Asp Phe Ser Ser Gln Ile Arg 1070 1075 1080 Ser Asn Pro Glu Leu Ala Ala Leu Phe Glu Ser Ile Gln Lys Asp 1085 1090 1095 Ser Ala Ser Ala Pro Ser Thr Asp Ser Met Glu Leu Ser 1100 1105 111088 443

<211> 443

<213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <400> 88

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Gln Glu Lys Glu Arg Lys Leu Glu Cys Leu Pro Pro Glu Pro

Ser Pro Asp Asp Pro Glu Ser Val Lys Ile Ile Phe Lys Leu Pro Asn 355 360 365 Asp Ser Arg Val Glu Arg Arg Phe His Phe Ser Gln Ser Leu Thr Val Ile His Asp Phe Leu Phe Ser Leu Lys Glu Ser Pro Glu Lys Phe Gln 385 390 395 400 Ile Glu Ala Asn Phe Pro Arg Arg Val Leu Pro Cys Ile Pro Ser Glu
405 410 415 Glu Trp Pro Asn Pro Pro Thr Leu Gln Glu Ala Gly Leu Ser His Thr 420 425 430 Glu Val Leu Phe Val Gln Asp Leu Thr Asp Glu

<210> <211> <212> <213>

89 306 PRT Homo sapiens

Met Ala Ser Pro Gly Cys Leu Trp Leu Leu Ala Val Ala Leu Leu Pro 1 10 15

Trp Thr Cys Ala Ser Arg Ala Leu Gln His Leu Asp Pro Pro Ala Pro

Leu Pro Leu Val Ile Trp His Gly Met Gly Asp Ser Cys Cys Asn Pro $35 \ \ 40 \ \ 45$

Leu Ser Met Gly Ala Ile Lys Lys Met Val Glu Lys Lys Ile Pro Gly

Ile Tyr Val Leu Ser Leu Glu Ile Gly Lys Thr Leu Met Glu Asp Val

Glu Asn Ser Phe Phe Leu Asn Val Asn Ser Gln Val Thr Thr Val Cys

Gln Ala Leu Ala Lys Asp Pro Lys Leu Gln Gln Gly Tyr Asn Ala Met 100 105 110

Gly Phe Ser Gln Gly Gln Phe Leu Arg Ala Val Ala Gln Arg Cys

Pro Ser Pro Pro Met Ile Asn Leu Ile Ser Val Gly Gly Gln His Gln

Gly val Phe Gly Leu Pro Arg Cys Pro Gly Glu Ser Ser His Ile Cys 145 150 160

Asp Phe Ile Arg Lys Thr Leu Asn Ala Gly Ala Tyr Ser Lys Val Val 165 170 175

Gln Glu Arg Leu Val Gln Ala Glu Tyr Trp His Asp Pro Ile Lys Glu

Asp val Tyr Arg Asn His Ser Ile Phe Leu Ala Asp Ile Asn Gln Glu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Gly Ile Asn Glu Ser Tyr Lys Lys Asn Leu Met Ala Leu Lys Lys Phe Val Met Val Lys Phe Leu Asn Asp Ser Ile Val Asp Pro Val Asp 225 230 235 240 Ser Glu Trp Phe Gly Phe Tyr Arg Ser Gly Gln Ala Lys Glu Thr Ile Pro Leu Gln Glu Thr Ser Leu Tyr Thr Gln Asp Arg Leu Gly Leu Lys 260 265 270Glu Met Asp Asn Ala Gly Gln Leu Val Phe Leu Ala Thr Glu Gly Asp 275 280 285 His Leu Gln Leu Ser Glu Glu Trp Phe Tyr Ala His Ile Ile Pro Phe

Leu Gly 305

<210> 90 <211> 461 <212> PRT <213> Home

<400>

Met Tyr Asn Thr Val Trp Ser Met Asp Arg Asp Asp Ala Asp Trp Arg Glu Val Met Met Pro Tyr Ser Thr Glu Leu Ile Phe Tyr Ile Glu Met Asp Pro Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Met Thr Ser Ala 35 40 45Val Pro Asn Gly Met Lys Asp Ser Ser Val Ser Leu Gln Asp Ala Glu Trp Tyr Trp Gly Asp Ile Ser Arg Glu Glu Val Asn Asp Lys Leu Arg 65 70 75Asp Met Pro Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met Gln Gly Asp Tyr Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu 100 105 110 Ile Lys Ile Tyr His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Asn Ser val val Glu Leu Ile Asn His Tyr His His Glu Ser Leu Ala Gln Tyr Asn Pro Lys Leu Asp Val Lys Leu Met Tyr Pro Val Ser Arg Tyr Gln Gln Asp Gln Leu Val Lys Glu Asp Asn Ile Asp Ala Val Gly Lys Leu Gln Glu Tyr His Ser Gln Tyr Gln Glu Lys Ser 180 185 190

Lys Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 195 200 205 Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys 210 220 Ile Phe Glu Glu Gln Cys His Thr Gln Glu Gln His Ser Lys Glu Tyr 225 230 235 240 Ile Glu Arg Phe Arg Arg Glu Gly Asn Glu Lys Glu Ile Glu Arg Ile Met Met Asn Tyr Asp Lys Leu Lys Ser Arg Leu Gly Glu Ile His Asp 260 270 Ser Lys Met Arg Leu Glu Gln Asp Leu Lys Lys Gln Ala Leu Asp Asn 275 280 285 Arg Glu Ile Asp Lys Lys Met Asn Ser Ile Lys Pro Asp Leu Ile Gln $290 \hspace{1.5cm} 295 \hspace{1.5cm} 300$ Leu Arg Lys Ile Arg Asp Gln His Leu Val Trp Leu Asn His Lys Gly Val Arg Gln Lys Arg Leu Asn Val Trp Leu Gly Ile Lys Asn Glu Asp 325 330 335 Ala Asp Glu Asn Tyr Phe Ile Asn Glu Glu Asp Glu Asn Leu Pro His 340 345 Tyr Asp Glu Lys Thr Trp Phe Val Glu Asp Ile Asn Arg Val Gln Ala 355 360 365 Glu Asp Leu Leu Tyr Gly Lys Pro Asp Gly Ala Phe Leu Ile Arg Glu 370 375 380Ser Ser Lys Lys Gly Cys Tyr Ala Cys Ser Val Val Ala Asp Gly Glu 385 390 395 400 Val Lys His Cys Val Ile Tyr Ser Thr Ala Arg Gly Tyr Gly Phe Ala 405 410 415Glu Pro Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr 420 425 430 Gln Gln Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Arg Leu 435 440 445 Ala Tyr Pro Val His Ala Gln Met Pro Ser Leu Cys Arg

Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala 40 45

<210> 91 <211> 724 <212> PRT <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
50 55 60

Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala 100 105 110 Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu $130 \hspace{1cm} 135 \hspace{1cm} 140$ Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu 145 150 160 Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met 165 170 175 Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser Glu Met Ile Ser 195 200 205 Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile Gln Leu Leu Lys 210 215 220 Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr Trp Leu Thr Leu 275 230 235 240 Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln Thr Ser Ser Lys 245 250 255 Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe Ser Pro Met Leu 260 265 270 Phe arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu Asn Leu Ile Lys 275 280 285 Val lle Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu Arg Gln Pro Ala Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr Val Ala Asn Asn 305 310 315 320 Gly Met Asn Asn Met Ser Leu Gln Asn Ala Glu Trp Tyr Trp Gly 325 330Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Ala Asp 345 Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met His Gly Asp Tyr . 355 360 365 Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Ile Phe His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Ser Ser 385 390 395 400



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser Leu Ala Gln Tyr 405 410 415Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val Ser Lys Tyr Gln 420 430 Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala Val Gly Lys Lys 435 440 445 Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser Arg Glu Tyr Asp 450 455 460 Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu Ile Gln Met Lys 465 470 475 480 Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu 485 490 495 Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr Ile Glu Lys Phe 500 505 510 Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile Met His Asn Tyr
515 520 525 Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp Ser Arg Arg 530 540Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr Arg Glu Ile Asp 545 550 555 Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln Leu Arg Lys Thr $565 \ \ \, 570 \ \ \, 575$ Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly Val Arg Gln Lys 580 585 590 Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu Asp Gln Tyr Ser 595 600 Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp Glu Lys Thr Trp 610 615 620 Asn val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn Leu Leu Arg Gly 625 630 635 640 Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys 645 650 655 Tyr Ala Cys Ser Val Val Asp Gly Glu Val Lys His Cys Val Ile 660 665 670 Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr 675 680 685 Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala 705 710 715 720

Gln Gln Arg Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Homo sapiens

<400> Met Ala Gly Pro Glu Gly Phe Gln Tyr Arg Ala Leu Tyr Pro Phe Arg 1 10 15 Arg Glu Arg Pro Glu Asp Leu Glu Leu Leu Pro Gly Asp Val Leu Val 20 30 Val Ser Arg Ala Ala Leu Gln Ala Leu Gly Val Ala Glu Gly Glu 35 40 45 Arg Cys Pro Gln Ser Val Gly Trp Met Pro Gly Leu Asn Glu Arg Thr 50 60 Arg Gln Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Phe Leu Gly Pro 65 70 75 80 Val Ala Leu Ala Arg Pro Gly Pro Arg Pro Arg Gly Pro Arg Pro Leu 85 90 95 Pro Ala Arg Pro Arg Asp Gly Ala Pro Glu Pro Gly Leu Thr Leu Pro 100 105 110 Asp Leu Pro Glu Gln Phe Ser Pro Pro Asp Val Ala Pro Pro Leu Leu 115 120 125 Val Lys Leu Val Glu Ala Ile Glu Arg Thr Gly Leu Asp Ser Glu Ser 130 135 140 His Tyr Arg Pro Glu Leu Pro Ala Pro Arg Thr Asp Trp Ser Leu Ser 145 150 160 Asp Val Asp Gln Trp Asp Thr Ala Ala Leu Ala Asp Gly Ile Lys Ser 165 170 175Phe Leu Leu Ala Leu Pro Ala Pro Leu Val Thr Pro Glu Ala Ser Ala 180 185 190 Glu Ala Arg Arg Ala Leu Arg Glu Ala Ala Gly Pro Val Gly Pro Ala 195 200 205 Leu Glu Pro Pro Thr Leu Pro Leu His Arg Ala Leu Thr Leu Arg Phe 210 225 220 Leu Leu Gln His Leu Gly Arg Val Ala Arg Arg Ala Pro Ala Leu Gly 225 230 235 Pro Ala Val Arg Ala Leu Gly Ala Thr Phe Gly Pro Leu Leu Leu Arg 245 250 Ala Pro Pro Pro Ser Ser Pro Pro Pro Gly Gly Ala Pro Asp Gly 265 270 Ser Glu Pro Ser Pro Asp Phe Pro Ala Leu Leu Val Glu Lys Leu Leu 275 280 285 Gln Glu His Leu Glu Glu Glu Val Ala Pro Pro Ala Leu Pro Pro Lys Pro Pro Lys Ala Lys Pro Ala Pro Thr Val Leu Ala Asn Gly Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Pro Pro Ser Leu Gln Asp Ala Glu Trp Tyr Trp Gly Asp Ile Ser 325 330 335 Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Pro Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Ser Lys Ile Gln Gly Glu Tyr Thr Leu Thr 355 360 365 Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Val Phe His Arg Asp $370 \hspace{0.5cm} 375 \hspace{0.5cm} 380$ Gly His Tyr Gly Phe Ser Glu Pro Leu Thr Phe Cys Ser Val Val Asp 385 390 395 Leu Ile Asn His Tyr Arg His Glu Ser Leu Ala Gln Tyr Asn Ala Lys 405 410 415Leu Asp Thr Arg Leu Leu Tyr Pro Val Ser Lys Tyr Gln Gln Asp Gln 420 425 430 Ile Val Lys Glu Asp Ser Val Glu Ala Val Gly Ala Gln Leu Lys Val 435 440 445Tyr His Gln Gln Tyr Gln Asp Lys Ser Arg Glu Tyr Asp Gln Leu Tyr 450 460 Glu Glu Tyr Thr Arg Thr Ser Gln Glu Leu Gln Met Lys Arg Thr Ala 465 470 475 480 Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu Gln Gly Gln 485 490 495 Thr Gln Glu Lys Cys Ser Lys Glu Tyr Leu Glu Arg Phe Arg Glu 500 505 510 Gly Asn Glu Lys Glu Met Gln Arg Ile Leu Leu Asn Ser Glu Arg Leu
515 520 525 Lys Ser Arg Ile Ala Glu Ile His Glu Ser Arg Thr Lys Leu Glu Gln 530 540 Gln Leu Arg Ala Gln Ala Ser Asp Asn Arg Glu Ile Asp Lys Arg Met 545 550 555 560 Asn Ser Leu Lys Pro Asp Leu Met Gln Leu Arg Lys Ile Arg Asp Gln 575Tyr Leu Val Trp Leu Thr Gln Lys Gly Ala Arg Gln Lys Lys Ile Asn 580 585 Glu Trp Leu Gly Ile Lys Asn Glu Thr Glu Asp Gln Tyr Ala Leu Met 595 600 605 Glu Asp Glu Asp Asp Leu Pro His His Glu Glu Arg Thr Trp Tyr Val Gly Lys Ile Asn Arg Thr Gln Ala Glu Glu Met Leu Ser Gly Lys Arg 625 630 635 640 Asp Gly Thr Phe Leu Ile Arg Glu Ser Ser Gln Arg Gly Cys Tyr Ala $645 \hspace{0.5cm} 650 \hspace{0.5cm} 655$

CVS Ser Val Val Val Asp Gly Asp Thr Lys His Cys Val Ile Tyr Arg

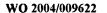
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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 660 665 670

Thr Ala Thr Gly Phe Gly Phe Ala Glu Pro Tyr Asn Leu Tyr Gly Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Ala Ser Leu Val Gln His Asn Asp Ala Leu Thr Val Thr Leu Ala His Pro Val Arg Ala Pro Gly 705 710 715 720 Pro Gly Pro Pro Pro Ala Ala Arg

93 534 PRT Homo sapiens

Met Ile Trp Tyr Ile Leu Ile Ile Gly Ile Leu Leu Pro Gln Ser Leu $10 \ 15$ His Thr Glu Lys Asp Leu Val Thr Ser Leu Lys Asp Tyr Ile Lys Ala 35 40 45 Glu Glu Asp Lys Leu Glu Gln Ile Lys Lys Trp Ala Glu Lys Leu Asp 50 60 Arg Leu Thr Ser Thr Ala Thr Lys Asp Pro Glu Gly Phe Val Gly His 65 70 75 80 Pro Val Asn Ala Phe Lys Leu Met Lys Arg Leu Asn Thr Glu Trp Ser Glu Leu Glu Asn Leu Val Leu Lys Asp Met Ser Asp Gly Phe Ile Ser 100 105Asn Leu Thr Ile Gln Arg Pro Val Leu Ser Asn Asp Glu Asp Gln Val Gly Ala Lys Ala Leu Leu Arg Leu Gln Asp Thr Tyr Asn Leu Asp 130 135 140 Thr Asp Thr Ile Ser Lys Gly Asn Leu Pro Gly Val Lys His Lys Ser 145 150 155 160 Phe Leu Thr Ala Glu Asp Cys Phe Glu Leu Gly Lys Val Ala Tyr Thr 165 170 175 Glu Ala Asp Tyr Tyr His Thr Glu Leu Trp Met Glu Gln Ala Leu Arg 180 185 190 Gln Leu Asp Glu Gly Glu Ile Ser Thr Ile Asp Lys Val Ser Val Leu 195 200 205 Asp Tyr Leu Ser Tyr Ala Val Tyr Gln Gln Gly Asp Leu Asp Lys Ala 210 220 Leu Leu Thr Lys Lys Leu Leu Glu Leu Asp Pro Glu His Gln Arg 225 230 235 240



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ala Asn Gly Asn Leu Lys Tyr Phe Glu Tyr Ile Met Ala Lys Glu Lys
245
250
255

Asp Val Asn Lys Ser Ala Ser Asp Asp Gln Ser Asp Gln Lys Thr Thr Pro Lys Lys Gly Val Ala Val Asp Tyr Leu Pro Glu Arg Gln Lys 275 280 285 Tyr Glu Met Leu Cys Arg Gly Glu Gly Ile Lys Met Thr Pro Arg Arg 290 295 300 Gln Lys Lys Leu Phe Cys Arg Tyr His Asp Gly Asn Arg Asn Pro Lys 305 310 315 320 Phe Ile Leu Ala Pro Ala Lys Gln Glu Asp Glu Trp Asp Lys Pro Arg Ile Ile Arg Phe His Asp Ile Ile Ser Asp Ala Glu Ile Glu Ile Val 340 345 350 Lys Asp Leu Ala Lys Pro Arg Leu Ser Arg Ala Thr Val His Asp Pro 355 360 365 Glu Thr Gly Lys Leu Thr Thr Ala Gln Tyr Arg Val Ser Lys Ser Ala 370 380 Trp Leu Ser Gly Tyr Glu Asn Pro Val Val Ser Arg Ile Asn Met Arg Ile Gln Asp Leu Thr Gly Leu Asp Val Ser Thr Ala Glu Glu Leu Gln
405 410 415 Val Ala Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro His Phe Asp Phe 420 425 430 Ala Arg Lys Asp Glu Pro Asp Ala Phe Lys Glu Leu Gly Thr Gly Asn 435 440 445 Arg Ile Ala Thr Trp Leu Phe Tyr Met Ser Asp Val Ser Ala Gly Gly 450 455 460 Ala Thr Val Phe Pro Glu Val Gly Ala Ser Val Trp Pro Lys Lys Gly 465 470 475 480 Thr Ala Val Phe Trp Tyr Asn Leu Phe Ala Ser Gly Glu Gly Asp Tyr 485 490 495Ser Thr Arg His Ala Ala Cys Pro Val Leu Val Gly Asn Lys Trp Val Ser Asn Lys Trp Leu His Glu Arg Gly Gln Glu Phe Arg Arg Pro Cys

Thr Leu Ser Glu Leu Glu 530

<210> 94 <211> 389 <212> PRT

<213> Homo sapiens

<400> 94

Met Leu Ser Leu Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln 10 15

Protein Complexes of Cellular networks underlying the development of cancer and other diseases.ST25.txt

Leu Gln Leu Ser Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn
20
25

Thr Pro Pro Ala Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala Arg Arg Ile Phe Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala Ala 50 60 Pro Gly Val Glu Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe 65 70 75 Val Ile Phe Pro Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys 90 95 Ala Glu Ala Ser Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp
100 105 110 Ile Gln His Trp Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser His Val Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn 130 135 140 Leu Val Glu Arg Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys 145 150 160 Phe Tyr Gly Phe Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr 165 170 175 Ser Leu Leu Ile Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe 180 185 190Leu Phe Asn Ala Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp 195 200 205 Trp Ala Leu Arg Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg Val Val Ala Phe Ala Ala Val Glu Gly Ile Phe Phe Ser Gly Ser Phe 225 230 235 240 Ala Ser Ile Phe Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr 245 250 Phe Ser Asn Glu Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe 260 265 270 Ala Cys Leu Met Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg 275 280 285 Val Arg Glu Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu Thr Glu Ala Leu Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met 305 310 315 Lys Gln Tyr Ile Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly Phe Ser Lys Val Phe Arg Val Glu Asn Pro Phe Asp Phe Met Glu Asn 340 345 Ile Ser Leu Glu Gly Lys Thr Asn Phe Phe Glu Lys Arg Val Gly Glu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 365

Tyr Gln Arg Met Gly Val Met Ser Ser Pro Thr Glu Asn Ser Phe Thr 370 380

Leu Asp Ala Asp Phe 385

<210> 95

<211> 794

<213> Homo sapiens

<400> 95

Met Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu Leu 10 15 15

Ser Leu Ala Ser Ala Ser Ser Asp Glu Glu Gly Ser Gln Asp Glu Ser

Leu Asp Ser Lys Thr Thr Leu Thr Ser Asp Glu Ser Val Lys Asp His $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Thr Thr Ala Gly Arg Val Val Ala Gly Gln Ile Phe Leu Asp Ser Glu 50 60

Glu Ser Glu Leu Glu Ser Ser Ile Gln Glu Glu Glu Asp Ser Leu Lys 70 75 80

Pro Asn Pro Glu Asn Lys Asp Tyr Glu Glu Pro Lys Lys Val Arg Lys

Pro Ala Leu Thr Ala Ile Glu Gly Thr Ala His Gly Glu Pro Cys His

Phe Pro Phe Leu Phe Leu Asp Lys Glu Tyr Asp Glu Cys Thr Ser Asp 130 140

Gly Arg Glu Asp Gly Arg Leu Trp Cys Ala Thr Thr Tyr Asp Tyr Lys 145 150 155 160

Ala Asp Glu Lys Trp Gly Phe Cys Glu Thr Glu Glu Glu Ala Ala Lys 165 170 175

Arg Arg Gln Met Gln Glu Ala Glu Met Met Tyr Gln Thr Gly Met Lys 180 185 190

Ile Leu Asn Gly Ser Asn Lys Lys Ser Gln Lys Arg Glu Ala Tyr Arg 195 200 205

Tyr Leu Gln Lys Ala Ala Ser Met Asn His Thr Lys Ala Leu Glu Arg 210 220

val Ser Tyr Ala Leu Leu Phe Gly Asp Tyr Leu Pro Gln Asn Ile Gln 225 230 235 240

Ala Ala Arg Glu Met Phe Glu Lys Leu Thr Glu Glu Gly Ser Pro Lys 255 255

Gly Gln Thr Ala Leu Gly Phe Leu Tyr Ala Ser Gly Leu Gly Val Asn

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ser Ser Gln Ala Lys Ala Leu Val Tyr Tyr Thr Phe Gly Ala Leu Gly
275 280 285

Gly Asn Leu Ile Ala His Met Val Leu Gly Tyr Arg Tyr Trp Ala Gly Ile Gly Val Leu Gln Ser Cys Glu Ser Ala Leu Thr His Tyr Arg Leu 305 310 315 320 Val Ala Asn His Val Ala Ser Asp Ile Ser Leu Thr Gly Gly Ser Val Val Gln Arg Ile Arg Leu Pro Asp Glu Val Glu Asn Pro Gly Met Asn 340 345 Ser Gly Met Leu Glu Glu Asp Leu Ile Gln Tyr Tyr Gln Phe Leu Ala 355 360 365 Glu Lys Gly Asp Val Gln Ala Gln Val Gly Leu Gly Gln Leu His Leu 370 380 His Gly Gly Arg Gly Val Glu Gln Asn His Gln Arg Ala Phe Asp Tyr Phe Asn Leu Ala Ala Asn Ala Gly Asn Ser His Ala Met Ala Phe Leu
405 410 415 Gly Lys Met Tyr Ser Glu Gly Ser Asp Ile Val Pro Gln Ser Asn Glu 420 425 430 Thr Ala Leu His Tyr Phe Lys Lys Ala Ala Asp Met Gly Asn Pro Val Gly Gln Ser Gly Leu Gly Met Ala Tyr Leu Tyr Gly Arg Gly Val Gln 450 455 460 . val Asn Tyr Asp Leu Ala Leu Lys Tyr Phe Gln Lys Ala Ala Glu Gln 465 470 475 480Gly Trp Val Asp Gly Gln Leu Gln Leu Gly Ser Met Tyr Tyr Asn Gly
485 490 495 Ile Gly Val Lys Arg Asp Tyr Lys Gln Ala Leu Lys Tyr Phe Asn Leu
500 505 510 Ala Ser Gln Gly Gly His Ile Leu Ala Phe Tyr Asn Leu Ala Gln Met 515 525 His Ala Ser Gly Thr Gly Val Met Arg Ser Cys His Thr Ala Val Glu 530 535 540 Leu Phe Lys Asn Val Cys Glu Arg Gly Arg Trp Ser Glu Arg Leu Met Thr Ala Tyr Asn Ser Tyr Lys Asp Gly Asp Tyr Asn Ala Ala Val Ile Gln Tyr Leu Leu Leu Ala Glu Gln Gly Tyr Glu Val Ala Gln Ser Asn 580 585 590 Ala Ala Phe Ile Leu Asp Gln Arg Glu Ala Ser Ile Val Gly Glu Asn 595 600 605 Glu Thr Tyr Pro Arg Ala Leu Leu His Trp Asn Arg Ala Ala Ser Gln 610 620

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gly Tyr Thr Val Ala Arg Ile Lys Leu Gly Asp Tyr His Phe Tyr Gly 625 630 635 Phe Gly Thr Asp Val Asp Tyr Glu Thr Ala Phe Ile His Tyr Arg Leu 645 650 655 Ala Ser Glu Gln Gln His Ser Ala Gln Ala Met Phe Asn Leu Gly Tyr 660 665 670Met His Glu Lys Gly Leu Gly Ile Lys Gln Asp Ile His Leu Ala Lys 675 680 Arg Phe Tyr Asp Met Ala Ala Glu Ala Ser Pro Asp Ala Gln Val Pro 690 700 Val Phe Leu Ala Leu Cys Lys Leu Gly Val Val Tyr Phe Leu Gln Tyr 705 710 725 720 Ile Arg Glu Thr Asn Ile Arg Asp Met Phe Thr Gln Leu Asp Met Asp 735 735 Gln Leu Leu Gly Pro Glu Trp Asp Leu Tyr Leu Met Thr Ile Ile Ala 740 745 750 Leu Leu Gly Thr Val Ile Ala Tyr Arg Gln Arg Gln His Gln Asp 755 760 765 Met Pro Ala Pro Arg Pro Pro Gly Pro Arg Pro Ala Pro Pro Gln Gln
770 775 780 Glu Gly Pro Pro Glu Gln Gln Pro Pro Gln 785

<210> <211> <212> <213> 96 583 PRT

Homo sapiens

<400>

Met Asp Leu Leu Pro Pro Lys Pro Lys Tyr Asn Pro Leu Arg Asn Glu 1 5 10 15 Ser Leu Ser Ser Leu Glu Glu Gly Ala Ser Gly Ser Thr Pro Pro Glu 20 25 30 Glu Leu Pro Ser Pro Ser Ala Ser Ser Leu Gly Pro Ile Leu Pro Pro 35 40 45 Leu pro Gly Asp Asp Ser Pro Thr Thr Leu Cys Ser Phe Phe Pro Arg Met Ser Asn Leu Arg Leu Ala Asn Pro Ala Gly Gly Arg Pro Gly Ser 65 70 80 Lys Gly Glu Pro Gly Arg Ala Ala Asp Asp Gly Glu Gly Ile Asp Gly 85 90 95 Ala Ala Met Pro Glu Ser Gly Pro Leu Pro Leu Gln Asp Met Asn Lys Leu Ser Gly Gly Gly Gly Arg Arg Thr Arg Val Glu Gly Gly Gln Leu Gly Gly Glu Glu Trp Thr Arg His Gly Ser Phe Val Asn Lys Pro

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.tXt 130 135 140

Thr Arg Gly Trp Leu His Pro Asn Asp Lys Val Met Gly Pro Gly Val 145 150 155 160 Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln Ser Met
165 170 175 Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu Ala Ile 180 185 190 Ser Leu Val Cys Glu Ala Val Pro Gly Ala Lys Gly Ala Thr Arg Arg 195 200 205 Arg Lys Pro Cys Ser Arg Pro Leu Ser Ser Ile Leu Gly Arg Ser Asn 210 225 220 Leu Lys Phe Ala Gly Met Pro Ile Thr Leu Thr Val Ser Thr Ser Ser 225 230 235 240 Leu Asn Leu Met Ala Ala Asp Cys Lys Gln Ile Ile Ala Asn His His 245 250 255 Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr Ala Glu 260 265 270 Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala Cys His 275 280 285 Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser Thr Ile 290 295 300 Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn Pro Pro 305 310 315 320 Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly Ser Ala 325 330 335 Trp Asp Glu Glu Glu Glu Pro Pro Asp His Gln Tyr Tyr Asn Asp 345 350 Arg Glu Gly Ala Ala Pro Gly Ala Ala Arg Pro Thr Ala Pro Asn Ala 370 380 Gln Thr Pro Ser His Leu Gly Ala Thr Leu Pro Val Gly Gln Pro Val 385 390 395 400 Gly Gly Asp Pro Glu Val Arg Lys Gln Met Pro Pro Pro Pro Cys 405 410 415 Pro Gly Arg Glu Leu Phe Asp Asp Pro Ser Tyr Val Asn Val Gln Asn 420 425 430 Leu ASP Lys Ala Arg Gln Ala Val Gly Gly Ala Gly Pro Pro Asn Pro 435 445 Ala Ile Asn Gly Ser Ala Pro Arg Asp Leu Phe Asp Met Lys Pro Phe 450 455 460 Glu ASP Ala Leu Arg Val Pro Pro Pro Pro Gln Ser Val Ser Met Ala 465 470 475 480

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Gln Leu Arg Gly Glu Pro Trp Phe His Gly Lys Leu Ser Arg Arg
485
490
495

Glu Ala Glu Ala Leu Leu Gln Leu Asn Gly Asp Phe Leu Val Arg Glu 505

Ser Thr Thr Thr Pro Gly Gln Tyr Val Leu Thr Gly Leu Gln Ser Gly 515

Gln Pro Lys His Leu Leu Leu Val Asp Pro Glu Gly Val Val Arg Thr 530 540

Lys Asp His Arg Phe Glu Ser Val Ser His Leu Ile Ser Tyr His Met 545 550 560

Asp Asn His Leu Pro Ile Ile Ser Ala Gly Ser Glu Leu Cys Leu Gln 575

Glm Pro Val Glu Arg Lys Leu 580

<210> 97 <211> 238

<212> PKI <213> Homo sapiens

<400> 97

Met Met Leu Met Ala Phe His Leu Tyr Leu Pro Met Val Glu Val Met 10^{10} Met 15^{10} Met Ser Tyr Leu Thr His Glu Phe Gly Arg Thr Leu Pro Phe Gly Ala Ser 25^{10} Arg Pro Tyr Lys Gln Met Gly Ala Gly Leu Leu Ser Gln Pro Val Gly 45^{10}

Leu Leu Ala Gly Gly Val Val Thr Ala Ile Ser Lys Ala Ala Gly Ala 50 60

Pro Ile Glu Trp Leu Lys Leu Leu Leu Gln Val Gln His Ala Thr Lys 65 70 75 80

Glu Ile Thr Thr Asp Lys Gln Tyr Lys His Ile Ile Asp Cys Val Val 85 90 95

Cys Ile Pro Lys Glu Glu Arg Val Leu Ser Phe Trp Arg Gly Ala Leu $100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}$

Asn Phe Ala Phe Glu Ile Ser Thr Ser Arg Ser Ser Trp Val Val Trp 115 120 125

Thr Arg Gly Pro Thr Phe Ser Thr Met Leu Gln Gly Thr Trp His Gln

Ala Cys Ala Gly Ala Thr Ser Leu Cys Phe Val Tyr Pro Leu Asp Phe 145 150 150 160

Val Cys Thr Asn Leu Pro Val Asp Val Gly Lys Ala Gly Ala Lys Arg 165 170 175

Arg Ile Lys Gly Leu His Gln Gly Phe Thr Met Ser Val Gln Gly Ile 195 200 205

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Ile Tyr Pro Ala Ala Tyr Phe Ser Ile Cys Asp Thr Ala Lys Gly 210 215

Met Leu Pro Asp Ser Lys Ser Thr Thr Ser Ser Ser Ala Glu 225 230 235

<210> 98 <211> 337 <212> PRT <213> Homo sapiens

Met Ser Leu Glu Glu Glu Glu Thr Gln Pro Gly Arg Leu Leu Gly $10 \ \ \, 10$

Arg Arg Asp Ala Val Pro Ala Phe Ile Glu Pro Asn Val Arg Phe Trp 20 30

Ile Thr Glu Arg Gln Ser Phe Ile Arg Arg Phe Leu Gln Trp Thr Glu 35 40 45

Leu Leu Asp Pro Thr Asn Val Phe Ile Ser Val Glu Ser Ile Glu Asn $50 \hspace{1.5cm} 60$

Ser Arg Gln Leu Leu Cys Thr Asn Glu Asp Val Ser Ser Pro Ala Ser 70 70

Ala Asp Gln Arg Ile Gln Glu Ala Trp Lys Arg Ser Leu Ala Thr Val 85 90 95

His Pro Asp Ser Ser Asn Leu Ile Pro Lys Leu Phe Arg Pro Ala Ala 100 105 110

Phe Leu Pro Phe Met Ala Pro Thr Val Phe Leu Ser Met Thr Pro Leu 115 120 125

Lys Gly Ile Lys Ser Val Ile Leu Pro Gln Val Phe Leu Cys Ala Tyr 130 140

Met Ala Ala Phe Asn Ser Ile Asn Gly Asn Arg Ser Tyr Thr Cys Lys 145 150 155 160

Pro Leu Glu Arg Ser Leu Leu Met Ala Gly Ala Val Ala Ser Ser Thr 165 170

Phe Leu Gly Val Ile Pro Gln Phe Val Gln Met Lys Tyr Gly Leu Thr 180 185 190

Gly Pro Trp Ile Lys Arg Leu Leu Pro Val Ile Phe Leu Val Gln Ala 195 200 205

Ser Gly Met Asn Val Tyr Met Ser Arg Ser Leu Glu Ser Ile Lys Gly 210 220

Ile Ala Val Met Asp Lys Glu Gly Asn Val Leu Gly His Ser Arg Ile 225 230 235

Ala Gly Thr Lys Ala Val Arg Glu Thr Leu Ala Ser Arg Ile Val Leu 245 250

Phe Gly Thr Ser Ala Leu Ile Pro Glu Val Phe Thr Tyr Phe Phe Lys 260 265 270

Arg Thr Gln Tyr Phe Arg Lys Asn Pro Gly Ser Leu Trp Ile Leu Lys

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 275 280 285

Leu Ser Cys Thr Val Leu Ala Met Gly Leu Met Val Pro Phe Ser Phe 290 300

Ser Ile Phe Pro Gln Ile Gly Gln Ile Gln Tyr Cys Ser Leu Glu Glu 305 310310315

Lys Ile Gln Ser Pro Thr Glu Glu Thr Glu Ile Phe Tyr His Arg Gly 325 330 335

٧a٦

<210> 99 <211> 654

<212> PRT <213> Homo sapiens

<400> 99

Met Asn Gly His Leu Glu Ala Glu Glu Gln Gln Asp Gln Arg Pro Asp 10 10 15

Gln Glu Leu Thr Gly Ser Trp Gly His Gly Pro Arg Ser Thr Leu Val

Arg Ala Lys Ala Met Ala Pro Pro Pro Pro Pro Leu Ala Ala Ser Thr 35 40 45

Pro Leu Leu His Gly Glu Phe Gly Ser Tyr Pro Ala Arg Gly Pro Arg 50 60

Phe Ala Leu Thr Leu Thr Ser Gln Ala Leu His Ile Gln Arg Leu Arg 65 70 75 80

Pro Lys Pro Glu Ala Arg Pro Arg Gly Gly Leu Val Pro Leu Ala Glu 85 90 95

Val Ser Gly Cys Cys Thr Leu Arg Ser Arg Ser Pro Ser Asp Ser Ala $100 \hspace{1cm} 105 \hspace{1cm} 110$

Ala Tyr Phe Cys Ile Tyr Thr Tyr Pro Arg Gly Arg Arg Gly Ala Arg 115 125 125

Arg Arg Ala Thr Arg Thr Phe Arg Ala Asp Gly Ala Ala Thr Tyr Glu 130 140

Glu Asn Arg Ala Glu Ala Gln Arg Trp Ala Thr Ala Leu Thr Cys Leu 145 150 155 160

Leu Arg Gly Leu Pro Leu Pro Gly Asp Gly Glu Ile Thr Pro Asp Leu 165 170 175

Leu Pro Arg Pro Pro Arg Leu Leu Leu Leu Val Asn Pro Phe Gly Gly 180 185 190

Arg Gly Leu Ala Trp Gln Trp Cys Lys Asn His Val Leu Pro Met Ile 195 200 205

Ser Glu Ala Gly Leu Ser Phe Asn Leu Ile Gln Thr Glu Arg Gln Asn 210 220

His Ala Arg Glu Leu Val Gln Gly Leu Ser Leu Ser Glu Trp Asp Gly 225 230 235 240 Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Val Thr Val Ser Gly Asp Gly Leu Leu His Glu Val Leu Asn Gly 245 250 255

Leu Leu Asp Arg Pro Asp Trp Glu Glu Ala Val Lys Met Pro Val Gly 265 270 Ile Leu Pro Cys Gly Ser Gly Asn Ala Leu Ala Gly Ala Val Asn Gln 275 280 285 His Gly Gly Phe Glu Pro Ala Leu Gly Leu Asp Leu Leu Leu Asn Cys 290 295 300 Ser Leu Leu Cys Arg Gly Gly Gly His Pro Leu Asp Leu Leu Ser 305 310 315 Val Thr Leu Ala Ser Gly Ser Arg Cys Phe Ser Phe Leu Ser Val Ala 325 330 335 Trp Gly Phe Val Ser Asp Val Asp Ile Gln Ser Glu Arg Phe Arg Ala 340 345 350 Leu Gly Ser Ala Arg Phe Thr Leu Gly Thr Val Leu Gly Leu Ala Thr $355 \hspace{1cm} 360 \hspace{1cm} 365$ Leu His Thr Tyr Arg Gly Arg Leu Ser Tyr Leu Pro Ala Thr Val Glu Pro Ala Ser Pro Thr Pro Ala His Ser Leu Pro Arg Ala Lys Ser Glu 385 390 395 400 Leu Thr Leu Thr Pro Asp Pro Ala Pro Pro Met Ala His Ser Pro Leu
405 410 415 His Arg Ser Val Ser Asp Leu Pro Leu Pro Leu Pro Gln Pro Ala Leu 420 425 430 Ala Ser Pro Gly Ser Pro Glu Pro Leu Pro Ile Leu Ser Leu Asn Gly 435 440 445 Gly Gly Pro Glu Leu Ala Gly Asp Trp Gly Gly Ala Gly Asp Ala Pro Leu Ser Pro Asp Pro Leu Leu Ser Ser Pro Pro Gly Ser Pro Lys Ala 465 470 475 480 Ala Leu His Ser Pro Val Ser Glu Gly Ala Pro Val Ile Pro Pro Ser Ser Gly Leu Pro Leu Pro Thr Pro Asp Ala Arg Val Gly Ala Ser Thr 500 505 510 Cys Gly Pro Pro Asp His Leu Leu Pro Pro Leu Gly Thr Pro Leu Pro 515 525 Pro Asp Trp Val Thr Leu Glu Gly Asp Phe Val Leu Met Leu Ala Ile 530 540 Ser Pro Ser His Leu Gly Ala Asp Leu Val Ala Ala Pro His Ala Arg 545 550 560 Phe ASP ASP Gly Leu Val His Leu Cys Trp Val Arg Ser Gly Ile Ser 575 Arg Ala Ala Leu Leu Arg Leu Phe Leu Ala Met Glu Arg Gly Ser His

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Phe Ser Leu Gly Cys Pro Gln Leu Gly Tyr Ala Ala Arg Ala Phe 595 600 605 Gln Val Glu Tyr Gly Pro Leu Gln Ala Gln Met His Pro Gly Ile Gly 625 630 635 Thr Leu Leu Thr Gly Pro Pro Gly Cys Pro Gly Arg Glu Pro

<400>

100 760 PRT Homo sapiens 100 Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu 10 15Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala 35 40 45Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly 50 60Ser Ile Cys Tyr Gly Thr Ile Ala Val Ile Val Phe Phe Leu Ile Gly $65 \hspace{1cm} 70 \hspace{1cm} 75 \hspace{1cm} 80$ Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro $100 \hspace{1cm} 105 \hspace{1cm} 110$ Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Gly Thr Ile 130 135 140 Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln 145 150 155 160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe 165 170 175 Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg 195 200 205

Leu val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys 210 220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys

Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu 260 265 270 Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe 275 280 285 Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly 290 295 300 Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln 305 310 315 320 Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr Ile Ser Arg Ala Ala Ala Glu Lys Leu Phe Gly Asn Met Glu Gly Asp 345 350 Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser 355 360 365 Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile 370 380 Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp 385 390 395 400 His Tyr Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala 405 410 415 Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Leu Lys Leu Ala Gln Met Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile 435 440 445 Ile Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr 450 455 460 Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr 465 470 475 480 Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn 500 : 505 510 Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp 515 520 525 Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp Thr ASP Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu 565 570 575 Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Ala Glu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn

595
600
605

Leu Asp Tyr Glu Arg Tyr Asp Ser Gln Leu Leu Ser Phe Val Arg Asp Leu Asn Gln Tyr Arg Asp Glo Asp Ile Lys Glu Met Gly Leu Ser Leu Gln G40

Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu Asp Phe G75 Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro G85

Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser G10 Asp Asp Asp Gly Asp Glu Thr Leu Pro Ala Leu Leu Glu Asp Leu Lys Leu Arg Lys Asp Asp Asp Gly Ala Asp Asp Glu Thr Leu Pro Ala Leu Leu Glu Asp Phe Arg Asp Asp Glo Leu Arg Cys Thr Asp Asp Asp Glo Ser Pro Ala Leu Leu Glu Asp Leu Lys Leu Arg Lys Thr Leu Ala Thr Trp Thr Ile Glo Gly Ala Ala Asp Ala Leu Ser Gly Asp Val Trp Asp Ile Asp Asp Glu Phe Tr60

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<400> 101

Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu

Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp

Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala

Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly

Ser Ile Cys Tyr Gly Thr Ile Ala Val Ile Val Phe Phe Leu Ile Gly

70

Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr

Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro

Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Ser Thr Ile

<210> 101

<211> 760

<212> PKI <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe 165 170 175 Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg 195 200 205 Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys 210 225 Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys 225 230 235 240 Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile 245 250 255 Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu 260 265 270 Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe 275 280 285 Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly 290 295 300 Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln 305 310 315 320 Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr 325 330 Ile Ser Arg Ala Ala Ala Glu Lys Leu Phe Gly Asn Met Glu Gly Asp 340 345 Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile 370 380 Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp 385 390 400 His Tyr Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala 415 Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Leu Lys Leu Ala Gln Met 420 430 Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile The Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr 450 460 Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr 465 470 470 480

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val 485 490 495

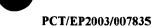
Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn 500 505 510 Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp 515 520 525 Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe 530 540 Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp 545 550 560 Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu 565 570 575 Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Glu 580 585 590 Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn 595 600 605 Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp 610 620Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln 625 630 635 Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu 645 650 655 Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys 660 670Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser 690 . 695 700 Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys 705 710 715 720 Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala 725 730 735 Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
740
750 Val Trp Asp Ile Asp Asn Glu Phe

<210> <211> <212> 102 1140 PRT

<213> Homo sapiens

Met Ser Tyr Asn Tyr Val Val Thr Ala Gln Lys Pro Thr Ala Val Asn 10 15

Gly Cys Val Thr Gly His Phe Thr Ser Ala Glu Asp Leu Asn Leu Leu



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ile Ala Lys Asn Thr Arg Leu Glu Ile Tyr Val Val Thr Ala Glu Gly
45

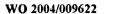
Leu Arg Pro Val Lys Glu Val Gly Met Tyr Gly Lys Ile Ala Val Met Glu Leu Phe Arg Pro Lys Gly Glu Ser Lys Asp Leu Leu Phe Ile Leu 65. 70 75 80 Thr Ala Lys Tyr Asn Ala Cys Ile Leu Glu Tyr Lys Gln Ser Gly Glu Ser Ile Asp Ile Ile Thr Arg Ala His Gly Asn Val Gln Asp Arg Ile 100 105 110 Gly Arg Pro Ser Glu Thr Gly Ile Ile Gly Ile Ile Asp Pro Glu Cys 115 120 125 Arg Met Ile Gly Leu Arg Leu Tyr Asp Gly Leu Phe Lys Val Ile Pro 130 135 140 Leu Asp Arg Asp Asn Lys Glu Leu Lys Ala Phe Asn Ile Arg Leu Glu 145 150 155 160 Glu Leu His Val Ile Asp Val Lys Phe Leu Tyr Gly Cys Gln Ala Pro 165 170 175 Thr Ile Cys Phe Val Tyr Gln Asp Pro Gln Gly Arg His Val Lys Thr 180 185 190 Tyr Glu Val Ser Leu Arg Glu Lys Glu Phe Asn Lys Gly Pro Trp Lys 195 200 205 Gln Glu Asn Val Glu Ala Glu Ala Ser Met Val Ile Ala Val Pro Glu 210 215 220 Pro Phe Gly Gly Ala Ile Ile Ile Gly Gln Glu Ser Ile Thr Tyr His Asn Gly Asp Lys Tyr Leu Ala Ile Ala Pro Pro Ile Ile Lys Gln Ser 245 250 255 Thr Ile Val Cys His Asn Arg Val Asp Pro Asn Gly Ser Arg Tyr Leu 260 265 270 Leu Gly Asp Met Glu Gly Arg Leu Phe Met Leu Leu Glu Lys Glu 275 280 285 Glu Gln Met Asp Gly Thr Val Thr Leu Lys Asp Leu Arg Val Glu Leu 290 295 300 Leu Gly Glu Thr Ser Ile Ala Glu Cys Leu Thr Tyr Leu Asp Asn Gly 305 310 315 320 val val Phe Val Gly Ser Arg Leu Gly Asp Ser Gln Leu Val Lys Leu 325 330 335 Asn val Asp Ser Asn Glu Gln Gly Ser Tyr val val Ala Met Glu Thr 340 345 350 Phe Thr Asn Leu Gly Pro Ile Val Asp Met Cys Val Val Asp Leu Glu 355 360 Arg Gln Gly Gln Gly Gln Leu Val Thr Cys Ser Gly Ala Phe Lys Glu



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gly Ser Leu Arg Ile Ile Arg Asn Gly Ile Gly Ile His Glu His Ala 385 390 395 400Ser Ile Asp Leu Pro Gly Ile Lys Gly Leu Trp Pro Leu Arg Ser Asp 405 410 415Pro Asn Arg Glu Thr Tyr Asp Thr Leu Val Leu Ser Phe Val Gly Gln 420 430 Thr Arg Val Leu Met Leu Asn Gly Glu Glu Val Glu Glu Thr Glu Leu 435 440 445 Met Gly Phe Val Asp Asp Gln Gln Thr Phe Phe Cys Gly Asn Val Ala 450 455 460 His Gln Gln Leu Ile Gln Ile Thr Ser Ala Ser Val Arg Leu Val Ser 465 470 475 480 Gln Glu Pro Lys Ala Leu Val Ser Glu Trp Lys Glu Pro Gln Ala Lys 485 490 495 Asn Ile Ser Val Ala Ser Cys Asn Ser Ser Gln Val Val Val Ala Val 500 505 510 Gly Arg Ala Leu Tyr Tyr Leu Gln Ile His Pro Gln Glu Leu Arg Gln 515 520 525 Ile Ser His Thr Glu Met Glu His Glu Val Ala Cys Leu Asp Ile Thr Pro Leu Gly Asp Ser Asn Gly Leu Ser Pro Leu Cys Ala Ile Gly Leu 545 550 555 560 Trp Thr Asp Ile Ser Ala Arg Ile Leu Lys Leu Pro Ser Phe Glu Leu 565 570 575 Leu His Lys Glu Met Leu Gly Gly Glu Ile Ile Pro Arg Ser Ile Leu 580 585 590 Met Thr Thr Phe Glu Ser Ser His Tyr Leu Leu Cys Ala Leu Gly Asp 595 600 605 Gly Ala Leu Phe Tyr Phe Gly Leu Asn Ile Glu Thr Gly Leu Leu Ser 610 615 620 Asp Arg Lys Lys Val Thr Leu Gly Thr Gln Pro Thr Val Leu Arg Thr Phe Arg Ser Leu Ser Thr Thr Asn Val Phe Ala Cys Ser Asp Arg Pro 655 Thr Val Ile Tyr Ser Ser Asn His Lys Leu Val Phe Ser Asn Val Asn 660 665 670 Leu Lys Glu Val Asn Tyr Met Cys Pro Leu Asn Ser Asp Gly Tyr Pro Asp Ser Leu Ala Leu Ala Asn Asn Ser Thr Leu Thr Ile Gly Thr Ile $690 \hspace{1cm} 695 \hspace{1cm} 700$ Asp Glu Ile Gln Lys Leu His Ile Arg Thr Val Pro Leu Tyr Glu Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Pro Arg Lys Ile Cys Tyr Gln Glu Val Ser Gln Cys Phe Gly Val Leu Ser Ser Arg Ile Glu Val Gln Asp Thr Ser Gly Gly Thr Thr Ala Leu 740 745 750 Arg Pro Ser Ala Ser Thr Gln Ala Leu Ser Ser Ser Val Ser Ser Ser 755 760 765 Lys Leu Phe Ser Ser Ser Thr Ala Pro His Glu Thr Ser Phe Gly Glu $770 \hspace{1cm} 775 \hspace{1cm} 780$ Glu Val Glu Val His Asn Leu Leu Ile Ile Asp Gln His Thr Phe Glu 785 790 795 800 Val Leu His Ala His Gln Phe Leu Gln Asn Glu Tyr Ala Leu Ser Leu 805 810 815 Val Ser Cys Lys Leu Gly Lys Asp Pro Asn Thr Tyr Phe Ile Val Gly 820 825 830 Thr Ala Met Val Tyr Pro Glu Glu Ala Glu Pro Lys Gln Gly Arg Ile 835 840 845 Val Val Phe Glm Tyr Ser Asp Gly Lys Leu Glm Thr Val Ala Glu Lys Glu Val Lys Gly Ala Val Tyr Ser Met Val Glu Phe Asn Gly Lys Leu 865 870 875 880 Leu Ala Ser Ile Asn Ser Thr Val Arg Leu Tyr Glu Trp Thr Thr Glu 885 890 895 Lys Asp Val Arg Thr Glu Cys Asn His Tyr Asn Asn Ile Met Ala Leu Tyr Leu Lys Thr Lys Gly Asp Phe Ile Leu Val Gly Asp Leu Met Arg Ser Val Leu Leu Ala Tyr Lys Pro Met Glu Gly Asn Phe Glu Glu 930 940 Ile Ala Arg Asp Phe Asn Pro Asn Trp Met Ser Ala Val Glu Ile Leu 945 950 960 Asp Asp Asp Asn Phe Leu Gly Ala Glu Asn Ala Phe Asn Leu Phe Val Cys Gln Lys Asp Ser Ala Ala Thr Thr Asp Glu Glu Arg Gln His Leu 980 985 Gln Glu Val Gly Leu Phe His Leu Gly Glu Phe Val Asn Val Phe Cys 995 1000 1005 His Gly Ser Leu Val Met Gln Asn Leu Gly Glu Thr Ser Thr Pro 1010 1020 Thr Gln Gly Ser Val Leu Phe Gly Thr Val Asn Gly Met Ile Gly Leu Val Thr Ser Leu Ser Glu Ser Trp Tyr Asn Leu Leu Leu Asp 1040 1050 Met Gln Asn Arg Leu Asn Lys Val Ile Lys Ser Val Gly Lys Ile



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 1055 1060 1065

Glu His Ser Phe Trp Arg Ser Phe His Thr Glu Arg Lys Thr Glu 1070 1080

Pro Ala Thr Gly Phe Ile Asp Gly Asp Leu Ile Glu Ser Phe Leu 1085 1090 1095

Asp Ile Ser Arg Pro Lys Met Gln Glu Val Val Ala Asn Leu Gln 1100 1110

Tyr Asp Asp Gly Ser Gly Met Lys Arg Glu Ala Thr Ala Asp Asp 1115 1120 1125

Leu Ile Lys Val Val Glu Glu Leu Thr Arg Ile His

<210> 103 <211> 243 <212> PRT <213> Homo sapiens

Met Ala Lys Val Glu Gln Val Leu Ser Leu Glu Pro Gln His Glu Leu 1 10 15

Lys Phe Arg Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu

Gly Asn Pro Thr Asp Arg Asn Val Cys Phe Lys Val Lys Thr Thr Ala 35 45

Pro Arg Arg Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Ala Gly 50 60

Ala Ser Ile Asn Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro

Asn Glu Lys Ser Lys His Lys Phe Met Val Gln Ser Met Phe Ala Pro

Thr Asp Thr Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Glu 100 105 110

Asp Leu Met Asp Ser Lys Leu Arg Cys Val Phe Glu Leu Pro Ala Glu 115 120 125

Asn Asp Lys Pro His Asp Val Glu Ile Asn Lys Ile Ile Ser Thr Thr

Ala Ser Lys Thr Glu Thr Pro Ile Val Ser Lys Ser Leu Ser Ser Ser 145 150 155 160

Leu Asp Asp Thr Glu Val Lys Lys Val Met Glu Glu Cys Lys Arg Leu 165 170 175

Gln Gly Glu val Gln Arg Leu Arg Glu Glu Asn Lys Gln Phe Lys Glu 180 185 190

Glu Asp Gly Leu Arg Met Arg Lys Thr Val Gln Ser Asn Ser Pro Ile

Ser Ala Leu Ala Pro Thr Gly Lys Glu Glu Gly Leu Ser Thr Arg Leu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Leu Ala Leu Val Val Leu Phe Phe Ile Val Gly Val Ile Gly Lys
225 230 235. 240

Ile Ala Leu

104 878

Homo sapiens <400> 104 Met Glu Gln Trp Arg Gln Cys Gly Arg Trp Leu Ile Asp Cys Lys Val Leu Pro Pro Asn His Arg Val. Val Trp Pro Ser Ala Val Val Phe Asp Leu Ala Gln Ala Leu Arg Asp Gly Val Leu Leu Cys Gln Leu Leu His Gln Met Ser Gln Phe Leu Cys Leu Lys Asn Ile Arg Thr Phe Leu Lys 65 70 75 80 Val Cys His Asp Lys Phe Gly Leu Arg Asn Ser Glu Leu Phe Asp Pro Phe Asp Leu Phe Asp Val Arg Asp Phe Gly Lys Val Ile Ser Ala Val 100 105 110 Ser Arg Leu Ser Leu His Ser Ile Ala Gln Asn Lys Gly Ile Arg Pro 115 120 125 Phe Pro Ser Glu Glu Thr Thr Glu Asn Asp Asp Asp Val Tyr Arg Ser 130 140 Leu Glu Glu Leu Ala Asp Glu His Asp Leu Gly Glu Asp Ile Tyr Asp 145 150 155 160 Cys Val Pro Cys Glu Asp Gly Gly Asp Asp Ile Tyr Glu Asp Ile Ile Lys Val Glu Val Gln Gln Pro Met Ile Arg Tyr Met Gln Lys Met Gly 180 185 190 Met Thr Glu Asp Asp Lys Arg Asn Cys Cys Leu Leu Glu Ile Gln Glu 195 200 205 Thr Glu Ala Lys Tyr Tyr Arg Thr Leu Glu Asp Ile Glu Lys Asn Tyr Met Ser Pro Leu Arg Leu Val Leu Ser Pro Ala Asp Met Ala Ala Val 225 230 235 240 Phe Ile Asn Leu Glu Asp Leu Ile Lys Val His His Ser Phe Leu Arg

Ala Ile Asp Val Ser Val Met Val Gly Gly Ser Thr Leu Ala Lys Val 260 265 270

Phe Leu Asp Phe Lys Glu Arg Leu Leu Ile Tyr Gly Glu Tyr Cys Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Met Glu His Ala Gln Asn Thr Leu Asn Gln Leu Leu Ala Ser Arg Glu Asp Phe Arg Gln Lys Val Glu Glu Cys Thr Leu Lys Val Gln Asp Gly Lys Phe Lys Leu Gln Asp Leu Leu Val Val Pro Met Gln Arg Val 325 330 335 Leu Lys Tyr His Leu Leu Leu Lys Glu Leu Leu Ser His Ser Ala Glu 340 345 350 Arg Pro Glu Arg Gln Gln Leu Lys Glu Ala Leu Glu Ala Met Gln Asp 355 360 365 Leu Ala Met Tyr Ile Asn Glu Val Lys Arg Asp Lys Glu Thr Leu Arg 370 380 Lys Ile Ser Glu Phe Gln Ser Ser Ile Glu Asn Leu Gln Val Lys Leu 385 390 395 400 Glu Glu Phe Gly Arg Pro Lys Ile Asp Gly Glu Leu Lys Val Arg Ser Ile Val Asn His Thr Lys Gln Asp Arg Tyr Leu Phe Leu Phe Asp Lys 420 425 430 Val Val Ile Val Cys Lys Arg Lys Gly Tyr Ser Tyr Glu Leu Lys Glu
435 440 445 Ile Ile Glu Leu Leu Phe His Lys Met Thr Asp Asp Pro Met Asn Asn 450 Lys Asp Val Lys Lys Ser His Gly Lys Met Trp Ser Tyr Gly Phe Tyr 465 470 475 480 Leu Ile His Leu Gln Gly Lys Gln Gly Phe Gln Phe Phe Cys Lys Thr 485 490 495 Glu Asp Met Lys Arg Lys Trp Met Glu Gln Phe Glu Met Ala Met Ser 500 505 510 Asn Ile Lys Pro Asp Lys Ala Asn Ala Asn His His Ser Phe Gln Met 515 520 525 Tyr Thr Phe Asp Lys Thr Thr Asn Cys Lys Ala Cys Lys Met Phe Leu 530 535 540 Arg Gly Thr Phe Tyr Gln Gly Tyr Met Cys Thr Lys Cys Gly Val Gly 545 550 560 Ala His Lys Glu Cys Leu Glu Val Ile Pro Pro Cys Lys Phe Thr Ser Pro Ala Asp Leu Asp Ala Ser Gly Ala Gly Pro Gly Pro Lys Met Val Ala val Gln Asn Tyr His Gly Asn Pro Ala Pro Pro Gly Lys Pro Val 595 600 605 Leu Thr Phe Gln Thr Gly Asp Val Leu Glu Leu Leu Arg Gly Asp Pro

Glu Ser Pro Trp Trp Glu Gly Arg Leu Val Gln Thr Arg Lys Ser Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 625 630 635 Tyr Phe Pro Ser Ser Ser Val Lys Pro Cys Pro Val Asp Gly Arg Pro 645 650 655 Pro Ile Ser Arg Pro Pro Ser Arg Glu Ile Asp Tyr Thr Ala Tyr Pro
660 665 670 Trp Phe Ala Gly Asn Met Glu Arg Gln Gln Thr Asp Asn Leu Leu Lys
675 680 685 Ser His Ala Ser Gly Thr Tyr Leu Ile Arg Glu Arg Pro Ala Glu Ala 690 695 700 Glu Arg Phe Ala Ile Ser Ile Lys Phe Asn Asp Glu Val Lys His Ile 705 710 720 720 Lys Val Val Glu Lys Asp Asn Trp Ile His Ile Thr Glu Ala Lys Lys 725 730 735 Phe Asp Ser Leu Leu Glu Leu Val Glu Tyr Tyr Gln Cys His Ser Leu 740 745 750 Lys Glu Ser Phe Lys Gln Leu Asp Thr Thr Leu Lys Tyr Pro Tyr Lys
755 760 765 Ser Arg Glu Arg Ser Ala Ser Arg Ala Ser Ser Arg Ser Pro Ala Ser 770 780 Cys Ala Ser Tyr Asn Phe Ser Phe Leu Ser Pro Gln Gly Leu Ser Phe 785 790 795 800 Ala Ser Gln Gly Pro Ser Ala Pro Phe Trp Ser Val Phe Thr Pro Arg 805 810 815 Val lle Gly Thr Ala Val Ala Arg Tyr Asn Phe Ala Ala Arg Asp Met 820 825 830 Arg Glu Leu Ser Leu Arg Glu Gly Asp Val Val Arg Ile Tyr Ser Arg 835 840 845 Ile Gly Gly Asp Gln Gly Trp Trp Lys Gly Glu Thr Asn Gly Arg Ile Gly Trp Phe Pro Ser Thr Tyr Val Glu Glu Glu Gly Ile Gln 865 870 875

Met Glu Pro Trp Lys Gln Cys Ala Gln Trp Leu Ile His Cys Lys Val Leu Pro Thr Asn His Arg Val Thr Trp Asp Ser Ala Gln Val Phe Asp 20 30 Leu Ala Gl
n Thr Leu Arg Asp Gly Val Leu Leu Cys Gl
n Leu Leu Asn 35 45 Asn Leu Arg Ala His Ser Ile Asn Leu Lys Glu Ile Asn Leu Arg Pro

<210> 105 <211> 847 <212> PRT <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Gln Met Ser Gln Phe Leu Cys Leu Lys Asn Ile Arg Thr Phe Leu Thr
65 70 75 80

Ala Cys Cys Glu Thr Phe Gly Met Arg Lys Ser Glu Leu Phe Glu Ala 85 90 95 Phe Asp Leu Phe Asp Val Arg Asp Phe Gly Lys Val Ile Glu Thr Leu 100 105 110 Ser Arg Leu Ser Arg Thr Pro Ile Ala Leu Ala Thr Gly Ile Arg Pro 115 120 125 Phe Pro Thr Glu Glu Ser Ile Asn Asp Glu Asp Ile Tyr Lys Gly Leu 130 135 140 Pro Asp Leu Ile Asp Glu Thr Leu Val Glu Asp Glu Glu Asp Leu Tyr 145 150 160 Asp Cys Val Tyr Gly Glu Asp Glu Gly Gly Glu Val Tyr Glu Asp Leu 165 170 175 Met Lys Ala Glu Glu Ala His Gln Pro Lys Cys Pro Glu Asn Asp Ile 180 185 190 Arg Ser Cys Cys Leu Ala Glu Ile Lys Gln Thr Glu Glu Lys Tyr Thr 195 200 205 Glu Thr Leu Glu Ser Ile Glu Lys Tyr Phe Met Ala Pro Leu Lys Arg 210 215 220 Phe Leu Thr Ala Ala Glu Phe Asp Ser Val Phe Ile Asn Ile Pro Glu 225 230 235 240 Leu Val Lys Leu His Arg Asn Leu Met Gln Glu Ile His Asp Ser Ile $245 \hspace{0.25cm} 250 \hspace{0.25cm} 255$ Val Asn Lys Asn Asp Gln Asn Leu Tyr Gln Val Phe Ile Asn Tyr Lys 260 265 270Glu Arg Leu Val Ile Tyr Gly Gln Tyr Cys Ser Gly Val Glu Ser Ala 275 280 285 Ile Ser Ser Leu Asp Tyr Ile Ser Lys Thr Lys Glu Asp Val Lys Leu 290 300Lys Leu Glu Glu Cys Ser Lys Arg Ala Asn Asn Gly Lys Phe Thr Leu Arg Asp Leu Leu Val Val Pro Met Gln Arg Val Leu Lys Tyr His Leu
325 330 335 Leu Leu Gln Glu Leu Val Lys His Thr Thr Asp Pro Thr Glu Lys Ala Asn Leu Lys Leu Ala Leu Asp Ala Met Lys Asp Leu Ala Gln Tyr Val Asn Glu Val Lys Arg Asp Asn Glu Thr Leu Arg Glu Ile Lys Gln Phe 370 375 380Gln Leu Ser Ile Glu Asn Leu Asn Gln Pro Val Leu Leu Phe Gly Arg 385 390 395 400 Pro Gln Gly Asp Gly Glu Ile Arg Ile Thr Thr Leu Asp Lys His Thr 405 410 415

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Gln Glu Arg His Ile Phe Leu Phe Asp Leu Ala Val Ile Val Cys 420 425 430 Lys Arg Lys Gly Asp Asn Tyr Glu Met Lys Glu Ile Ile Asp Leu Gln $435\,$ Gln Tyr Lys Ile Ala Asn Asn Pro Thr Thr Asp Lys Glu Asn Lys Lys 450 455 460 Trp Ser Tyr Gly Phe Tyr Leu Ile His Thr Gln Gly Gln Asn Gly Leu 465 470 475 480 Glu Phe Tyr Cys Lys Thr Lys Asp Leu Lys Lys Lys Trp Leu Glu Gln
485 490 495 Phe Glu Met Ala Leu Ser Asn Ile Arg Pro Asp Tyr Ala Asp Ser Asn 500 505 Phe His Asp Phe Lys Met His Thr Phe Thr Arg Val Thr Ser Cys Lys 515 520 525 Val Cys Gln Met Leu Leu Arg Gly Thr Phe Tyr Gln Gly Tyr Leu Cys 530 540 Phe Lys Cys Gly Ala Arg Ala His Lys Glu Cys Leu Gly Arg Val Asp 545 550 555 Asn Cys Gly Arg Val Asn Ser Gly Glu Gln Gly Thr Leu Lys Leu Pro 565 570 575 Glu Lys Arg Thr Asn Gly Leu Arg Arg Thr Pro Lys Gln Val Asp Pro Gly Leu Pro Lys Met Gln Val Ile Arg Asn Tyr Ser Gly Thr Pro Pro 595 600 605 Pro Ala Leu His Glu Gly Pro Pro Leu Gln Leu Gln Ala Gly Asp Thr 610 620 Val Glu Leu Leu Lys Gly Asp Ala His Ser Leu Phe Trp Gln Gly Arg 625 630 635 Asn Leu Ala Ser Gly Glu Val Gly Phe Phe Pro Ser Asp Ala Val Lys 645 650 655Pro Cys Pro Cys Val Pro Lys Pro Val Asp Tyr Ser Cys Gln Pro Trp 660 665 670 Tyr Ala Gly Ala Met Glu Arg Leu Gln Ala Glu Thr Glu Leu Ile Asn $675 \hspace{1.5cm} 685$ Arg val Asn Ser Thr Tyr Leu Val Arg His Arg Thr Lys Glu Ser Gly 690 695 700 Glu Tyr Ala Ile Ser Ile Lys Tyr Asn Asn Glu Ala Lys His Ile Lys 705 710 715 720 Ile Leu Thr Arg Asp Gly Phe Phe His Ile Ala Glu Asn Arg Lys Phe 725 730 735'Lys Ser Leu Met Glu Leu Val Glu Tyr Tyr Lys His His Ser Leu Lys 740 745 750

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Gly Phe Arg Thr Leu Asp Thr Thr Leu Gln Phe Pro Tyr Lys Glu
755 760 765

Pro Glu His Ser Ala Gly Gln Arg Gly Asn Arg Ala Gly Asn Ser Leu 770 780 Leu Ser Pro Lys Val Leu Gly Ile Ala Ile Ala Arg Tyr Asp Phe Cys 785 790 795Ala Arg Asp Met Arg Glu Leu Ser Leu Leu Lys Gly Asp Val Val Lys 810 815 Ile Tyr Thr Lys Met Ser Ala Asn Gly Trp Trp Arg Gly Glu Val Asn Gly Arg Val Gly Trp Phe Pro Ser Thr Tyr Val Glu Glu Asp Glu 835 840 845

106 1121 PRT <210> <211> <212>

Homo sapiens

106 Met Asp Ala Leu Glu Asp Tyr Val Trp Pro Arg Ala Thr Ser Glu Leu $1 \ \ \, 10 \ \ \, 15$ Ile Leu Leu Pro Val Thr Gly Leu Glu Cys Val Gly Asp Arg Leu Leu 20 30 Ala Gly Glu Gly Pro Asp Val Leu Val Tyr Ser Leu Asp Phe Gly Gly His Leu Arg Met Ile Lys Arg Val Gln Asn Leu Leu Gly His Tyr Leu
50 55 60 Ile His Gly Phe Arg Val Arg Pro Glu Pro Asn Gly Asp Leu Asp Leu 65 70 75 . 80Glu Ala Met Val Ala Val Phe Gly Ser Lys Gly Leu Arg Val Val Lys 85 90 95 Ile Ser Trp Gly Gln Gly His Phe Trp Glu Leu Trp Arg Ser Gly Leu Trp Asn Met Ser Asp Trp Ile Trp Asp Ala Arg Trp Leu Glu Gly Asn 115 120 125 Ile Ala Leu Ala Leu Gly His Asn Ser Val Val Leu Tyr Asp Pro Val 130 135 140 Val Gly Cys Ile Leu Gln Glu Val Pro Cys Thr Asp Arg Cys Thr Leu 145 150 160

Ala Gly Ala Val Ser Asn Gln Leu Leu Val Trp Tyr Pro Ala Thr Ala 180 185 190 Leu Ala Asp Asn Lys Pro Val Ala Pro Asp Arg Arg Ile Ser Gly His 195 200 205 Val Gly Ile Ile Phe Ser Met Ser Tyr Leu Glu Ser Lys Gly Leu Leu 210 215 220

Ser Ser Ala Cys Leu Ile Gly Asp Ala Trp Lys Glu Leu Thr Ile Val

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Thr Ala Ser Glu Asp Arg Ser Val Arg Ile Trp Lys Val Gly Asp Leu Arg Val Pro Gly Gly Arg Val Gln Asn Ile Gly His Cys Phe Gly His Ser Ala Arg Val Trp Gln Val Lys Leu Leu Glu Asn Tyr Leu Ile 260 265 270 Ser Ala Gly Glu Asp Cys Val Cys Leu Val Trp Ser His Glu Gly Glu 275 280 285 Ile Leu Gln Ala Phe Arg Gly His Gln Gly Arg Gly Ile Arg Ala Ile Ala Ala His Glu Arg Gln Ala Trp Val Ile Thr Gly Gly Asp Asp Ser 305 $$ 310 $$ 315 $$ 320 Gly Ile Arg Leu Trp His Leu Val Gly Arg Gly Tyr Arg Gly Leu Gly
325 330 335 Val Ser Ala Leu Cys Phe Lys Ser Arg Ser Arg Pro Gly Thr Leu Lys 340 345 350 Ala Val Thr Leu Ala Gly Ser Trp Arg Leu Leu Ala Val Thr Asp Thr 355 360 365 Gly Ala Leu Tyr Leu Tyr Asp Val Glu Val Lys Cys Trp Glu Gln Leu 370 380 Leu Glu Asp Lys His Phe Gln Ser Tyr Cys Leu Leu Glu Ala Ala Pro 385 390 395 400 Gly Pro Glu Gly Phe Gly Leu Cys Ala Met Ala Asn Gly Glu Gly Arg 405 410 415Val Lys Val Val Pro Ile Asn Thr Pro Thr Ala Ala Val Asp Gln Thr Leu Phe Pro Gly Lys Val His Ser Leu Ser Trp Ala Leu Arg Gly Tyr 435 440 445 Glu Glu Leu Leu Leu Leu Ala Ser Gly Pro Gly Gly Val Val Ala Cys 450 455 460 Leu Glu Ile Ser Ala Ala Pro Ser Gly Lys Ala Ile Phe Val Lys Glu 465 470 475 480 Arg Cys Arg Tyr Leu Leu Pro Pro Ser Lys Gln Arg Trp His Thr Cys
485 490 495 Ser Ala Phe Leu Pro Pro Gly Asp Phe Leu Val Cys Gly Asp Arg Arg 500 505 Gly Ser Val Leu Leu Phe Pro Ser Arg Pro Gly Leu Leu Lys Asp Pro 515 520 525 Gly val Gly Gly Lys Ala Arg Ala Gly Ala Gly Ala Pro Val Val Gly Ser Gly Ser Ser Gly Gly Gly Asn Ala Phe Thr Gly Leu Gly Pro Val Ser Thr Leu Pro Ser Leu His Gly Lys Gln Gly Val Thr Ser Val Thr

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
565 570 575 Cys His Gly Gly Tyr Val Tyr Thr Thr Gly Arg Asp Gly Ala Tyr Tyr 580 585 590 Gln Leu Phe Val Arg Asp Gly Gln Leu Gln Pro Val Leu Arg Gln Lys 595 600 605 Ser Cys Arg Gly Met Asn Trp Leu Ala Gly Leu Arg Ile Val Pro Asp Gly Ser Met Val Ile Leu Gly Phe His Ala Asn Glu Phe Val Val Trp $625 \qquad \qquad 630 \qquad \qquad 635 \qquad \qquad 640$ Asn Pro Arg Ser His Glu Lys Leu His Ile Val Asn Cys Gly Gly Gly 655 His Arg Ser Trp Ala Phe Ser Asp Thr Glu Ala Ala Met Ala Phe Ala 660 670 Tyr Leu Lys Asp Gly Asp Val Met Leu Tyr Arg Ala Leu Gly Gly Cys 675 680 685 Thr Arg Pro His Val Ile Leu Arg Glu Gly Leu His Gly Arg Glu Ile 690 695 700 Thr Cys Val Lys Arg Val Gly Thr Ile Thr Leu Gly Pro Glu Tyr Gly 705 710 715 720 Val Pro Ser Phe Met Gln Pro Asp Asp Leu Glu Pro Gly Ser Glu Gly 725 730 735 Pro Asp Leu Thr Asp Ile Val Ile Thr Cys Ser Glu Asp Thr Thr Val 740 745 750 Cys Val Leu Ala Leu Pro Thr Thr Thr Gly Ser Ala His Ala Leu Thr Ala Val Cys Asn His Ile Ser Ser Val Arg Ala Val Ala Val Trp Gly
770 780 Ile Gly Thr Pro Gly Gly Pro Gln Asp Pro Gln Pro Gly Leu Thr Ala 785 790 795 800 His Val Val Ser Ala Gly Gly Arg Ala Glu Met His Cys Phe Ser Ile 815Met Val Thr Pro Asp Pro Ser Thr Pro Ser Arg Leu Ala Cys His Val Met His Leu Ser Ser His Arg Leu Asp Glu Tyr Trp Asp Arg Gln Arg 835 840 Asn arg His arg Met Val Lys Val Asp Pro Glu Thr Arg Tyr Met Ser Leu Ala Val Cys Glu Leu Asp Gln Pro Gly Leu Gly Pro Leu Val Ala 865 870 875 880 Ala Ala Cys Ser Asp Gly Ala Val Arg Leu Phe Leu Leu Gln Asp Ser Gly Arg Ile Leu Gln Leu Leu Ala Glu Thr Phe His His Lys Arg Cys

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Val Leu Lys Val His Ser Phe Thr His Glu Ala Pro Asn Gln Arg Arg
915
920
925

Arg Leu Leu Cys Ser Ala Ala Thr Asp Gly Ser Leu Ala Phe Trp 930 940

Asp Leu Thr Thr Met Leu Asp His Asp Ser Thr Val Leu Glu Pro Pro 945 950 955 960

Val Asp Pro Gly Leu Pro Tyr Arg Leu Gly Thr Pro Ser Leu Thr Leu 965 970 975

Gln Ala His Ser Cys Gly Ile Asn Ser Leu His Thr Leu Pro Thr Arg

Glu Gly His His Leu Val Ala Ser Gly Ser Glu Asp Gly Ser Leu His 995 1000 1005

Val Phe Val Leu Ala Val Glu Met Leu Gln Leu Glu Glu Ala Val 1010 1020

Gly Glu Ala Gly Leu Val Pro Gln Leu Arg Val Leu Glu Glu Tyr 1025 1030 1035

Ser Val Pro Cys Ala His Ala Ala His Val Thr Gly Leu Lys Ile 1040 1050

Leu Ser Pro Ser Ile Met Val Ser Ala Ser Ile Asp Gln Arg Leu 1055 1060 1065

Thr Phe Trp Arg Leu Gly His Gly Glu Pro Thr Phe Met Asn Ser 1070

Thr Val Phe His Val Pro Asp Val Ala Asp Met Asp Cys Trp Pro 1085 1090 1095

Val Ser Pro Glu Phe Gly His Arg Cys Ala Leu Gly Gly Gln Gly 1100 1110

Leu Glu Val Tyr Asn Trp Tyr Asp 1115 1120

<210> 107

<211> 79 <212> PRT

<213> Homo sapiens

<400> 107

Met Ala Ala Ser Gly Pro Gly Cys Arg Ser Trp Cys Leu Cys Pro Glu $1 \ \ \, 10 \ \ \, 15$

Val pro Ser Ala Thr Phe Phe Thr Ala Leu Leu Ser Leu Leu Val Ser

Gly Pro Arg Leu Phe Leu Leu Gln Gln Pro Leu Ala Pro Ser Gly Leu $35 ext{ } 40 ext{ } 45$

Thr Leu Lys Ser Glu Ala Leu Arg Asn Trp Gln Ala Thr Met Glu Gly

Gly val Arg Ile Thr Ala Glu Glu Thr Gly Thr Gln Ser Val Lys 65 70 75

<210> 108 <211> 801 Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Homo sapiens

<400> 108 Met Leu Gln Asn Val Thr Pro His Asn Lys Leu Pro Gly Glu Gly Asn Ala Gly Leu Gly Leu Gly Pro Glu Ala Ala Pro Gly Lys Arg Ile Arg Lys Pro Ser Leu Leu Tyr Glu Gly Phe Glu Ser Pro Thr Met 35 40 45Ala Ser Val Pro Ala Leu Gln Leu Thr Pro Ala Asn Pro Pro Pro 50 $\,$ 60 $\,$ Glu Val Ser Asn Pro Lys Lys Pro Gly Arg Val Thr Asn Gln Leu Gln Tyr Leu His Lys Val Val Met Lys Ala Leu Trp Lys His Gln Phe Ala 85 90 95 Trp Pro Phe Arg Gln Pro Val Asp Ala Val Lys Leu Gly Leu Pro Asp 100 105 110 Tyr His Lys Ile Ile Lys Gln Pro Met Asp Met Gly Thr Ile Lys Arg 115 120 125 Arg Leu Glu Asn Asn Tyr Tyr Trp Ala Ala Ser Glu Cys Met Gln Asp 130 135 140 Phe Asn Thr Met Phe Thr Asn Cys Tyr Ile Tyr Asn Lys Pro Thr Asp 145 150 155 160 Asp Ile Val Leu Met Ala Gln Thr Leu Glu Lys Ile Phe Leu Gln Lys 165 170 175 Val Ala Ser Met Pro Gln Glu Glu Gln Glu Leu Val Val Thr Ile Pro 180 185 190 Lys Asn Ser His Lys Lys Gly Ala Lys Leu Ala Ala Leu Gln Gly Ser 195 200 205 Val Thr Ser Ala His Gln Val Pro Ala Val Ser Ser Val Ser His Thr 210 215 220 Ala Leu Tyr Thr Pro Pro Pro Glu Ile Pro Thr Thr Val Leu Asn Ile 225 230 235 240 Pro His Pro Ser Val Ile Ser Ser Pro Leu Leu Lys Ser Leu His Ser 245 250 255 Ala Gly Pro Pro Leu Leu Ala Val Thr Ala Ala Pro Pro Ala Gln Pro 260 265 270 Leu Ala Lys Lys Lys Gly Val Lys Arg Lys Ala Asp Thr Thr Thr Pro 275 280 285 Thr Pro Thr Ala Ile Leu Ala Pro Gly Ser Pro Ala Ser Pro Pro Gly 290 295 300 Ser Leu Glu Pro Lys Ala Ala Arg Leu Pro Pro Met Arg Arg Glu Ser 305 310 315 320 Gly Arg Pro Ile Lys Pro Pro Arg Lys Asp Leu Pro Asp Ser Gln Gln Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln His Gln Ser Ser Lys Lys Gly Lys Leu Ser Glu Gln Leu Lys His Cys Asn Gly Ile Leu Lys Glu Leu Leu Ser Lys Lys His Ala Ala Tyr 355 360 365 Ala Trp Pro Phe Tyr Lys Pro Val Asp Ala Ser Ala Leu Gly Leu His 370 380 ASP Tyr His ASP Ile Ile Lys His Pro Met ASP Leu Ser Thr Val Lys 385 390 395 400 Arg Lys Met Glu Asn Arg Asp Tyr Arg Asp Ala Gln Glu Phe Ala Ala Asp Val Arg Leu Met Phe Ser Asn Cys Tyr Lys Tyr Asn Pro Pro Asp 420 430 ·His Asp Val Val Ala Met Ala Arg Lys Leu Gln Asp Val Phe Glu Phe Arg Tyr Ala Lys Met Pro Asp Glu Pro Leu Glu Pro Gly Pro Leu Pro 450 460 val Ser Thr Ala Met Pro Pro Gly Leu Ala Lys Ser Ser Ser Glu Ser 465 470 475 480 Ser Ser Glu Glu Ser Ser Ser Glu Ser Ser Glu Glu Glu Glu Glu 495 Glu Asp Glu Glu Glu Glu Glu Glu Ser Glu Ser Ser Asp Ser 500 505 510 Glu Glu Glu Arg Ala His Arg Leu Ala Glu Leu Gln Glu Gln Leu Arg 515 520 525 Ala Val His Glu Gln Leu Ala Ala Leu Ser Gln Gly Pro Ile Ser Lys 530 535 540 Pro Lys Arg Lys Arg Glu Lys Lys Glu Lys Lys Lys Lys Arg Lys Ala 545 550 555 Glu Lys His Arg Gly Arg Ala Gly Ala Asp Glu Asp Asp Lys Gly Pro 575 Arg Ala Pro Arg Pro Pro Gln Pro Lys Lys Ser Lys Lys Ala Ser Gly 585 Ser Gly Gly Gly Ser Ala Ala Leu Gly Pro Ser Gly Phe Gly Pro Ser 595 600 605 Gly Gly Ser Gly Thr Lys Leu Pro Lys Lys Ala Thr Lys Thr Ala Pro 610 620 Pro Ala Leu Pro Thr Gly Tyr Asp Ser Glu Glu Glu Glu Glu Ser Arg 625 630 635 640 Pro Met Ser Tyr Asp Glu Lys Arg Gln Leu Ser Leu Asp Ile Asn Lys 645 650 655 Leu pro Gly Glu Lys Leu Gly Arg Val Val His Ile Ile Gln Ala Arg 660 665 670

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Pro Ser Leu Arg Asp Ser Asn Pro Glu Glu Ile Glu Ile Asp Phe 675 680 685

Glu Thr Leu Lys Pro Ser Thr Leu Arg Glu Leu Glu Arg Tyr Val Leu 690 695 700 Ser Cys Leu Arg Lys Lys Pro Arg Lys Pro Tyr Thr Ile Lys Lys Pro 705 710 715 720 Val Gly Lys Thr Lys Glu Glu Leu Ala Leu Glu Lys Lys Arg Glu Leu 725 730 735 Glu Lys Arg Leu Gln Asp Val Ser Gly Gln Leu Asn Ser Thr Lys Lys Pro Pro Lys Lys Ala Asn Glu Lys Thr Glu Ser Ser Ser Ala Gln Gln 755 760 765 Ser Ser Ser Ser Ser Ser Ser Ser Ser Asp Thr Ser Asp Ser Asp Ser 785 790 795

<210> <211> <212> 109 1362 PRT

Gly

Homo sapiens

<400> 109

Met Ser Ala Glu Ser Gly Pro Gly Thr Arg Leu Arg Asn Leu Pro Val

Met Gly Asp Gly Leu Glu Thr Ser Gln Met Ser Thr Thr Gln Ala Gln

Ala Gln Pro Gln Pro Ala Asn Ala Ala Ser Thr Asn Pro Pro Pro Pro 35 40 45

Glu Thr Ser Asn Pro Asn Lys Pro Lys Arg Gln Thr Asn Gln Leu Gln
50 55 60

Tyr Leu Leu Arg Val Val Leu Lys Thr Leu Trp Lys His Gln Phe Ala

Trp Pro Phe Gln Gln Pro Val Asp Ala Val Lys Leu Asn Leu Pro Asp 90 95

Tyr Tyr Lys Ile Ile Lys Thr Pro Met Asp Met Gly Thr Ile Lys Lys $100 ext{ } 105 ext{ } 110$

Arg Leu Glu Asn Asn Tyr Tyr Trp Asn Ala Gln Glu Cys Ile Gln Asp 115 120 125

Phe Asn Thr Met Phe Thr Asn Cys Tyr Ile Tyr Asn Lys Pro Gly Asp 130 135 140

Asp Ile Val Leu Met Ala Glu Ala Leu Glu Lys Leu Phe Leu Gln Lys 145 150 160

Ile Asn Glu Leu Pro Thr Glu Glu Thr Glu Ile Met Ile Val Gln Ala 165 170 175

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Gly Arg Gly Arg Gly Arg Lys Glu Thr Gly Thr Ala Lys Pro Gly 180 185 val Ser Thr val Pro Asn Thr Thr Gln Ala Ser Thr Pro Pro Gln Thr 195 200 205 Gln Thr Pro Gln Pro Asn Pro Pro Pro Val Gln Ala Thr Pro His Pro 210 225 220 Phe Pro Ala Val Thr Pro Asp Leu Ile Val Gln Thr Pro Val Met Thr 225 230 235 240 Val Val Pro Pro Gln Pro Leu Gln Thr Pro Pro Pro Val Pro Pro Gln 245 250 255 Pro Gln Pro Pro Pro Ala Pro Ala Pro Gln Pro Val Gln Ser His Pro 260 265 270 Pro Ile Ile Ala Ala Thr Pro Gln Pro Val Lys Thr Lys Lys Gly Val 275 280 285 Lys Arg Lys Ala Asp Thr Thr Thr Pro Thr Thr Ile Asp Pro Ile His Glu Pro Pro Ser Leu Pro Pro Glu Pro Lys Thr Thr Lys Leu Gly Gln 305 310 315 320 Arg Arg Glu Ser Ser Arg Pro Val Lys Pro Pro Lys Lys Asp Val Pro 325 330 335 Asp Ser Gln Gln His Pro Ala Pro Glu Lys Ser Ser Lys Val Ser Glu Gln Leu Lys Cys Cys Ser Gly Ile Leu Lys Glu Met Phe Ala Lys Lys 355 360 365 His Ala Ala Tyr Ala Trp Pro Phe Tyr Lys Pro Val Asp Val Glu Ala 370 375 380 Leu Gly Leu His Asp Tyr Cys Asp Ile Ile Lys His Pro Met Asp Met 385 390 395 Ser Thr Ile Lys Ser Lys Leu Glu Ala Arg Glu Tyr Arg Asp Ala Gln 405 410 415Glu Phe Gly Ala Asp Val Arg Leu Met Phe Ser Asn Cys Tyr Lys Tyr 420 425 430 Asn Pro Pro Asp His Glu Val Val Ala Met Ala Arg Lys Leu Gln Asp 435 440 445 Val Phe Glu Met Arg Phe Ala Lys Met Pro Asp Glu Pro Glu Glu Pro 450 460 Val Val Ala Val Ser Ser Pro Ala Val Pro Pro Pro Thr-Lys Val Val 465 470 475 Asp Ser Ser Thr Asp Asp Ser Glu Glu Glu Arg Ala Gln Arg Leu Ala

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Leu Gln Glu Gln Leu Lys Ala Val His Glu Gln Leu Ala Ala Leu
515 520 525

Ser Gln Pro Gln Gln Asn Lys Pro Lys Lys Glu Lys Asp Lys Lys 530 540 Glu Lys Lys Lys Glu Lys His Lys Arg Lys Glu Glu Val Glu Glu Asn 545 550 560 Lys Lys Ser Lys Ala Lys Glu Pro Pro Pro Lys Lys Thr Lys Lys Asn 565 570 575 Asn Ser Ser Asn Ser Asn Val Ser Lys Lys Glu Pro Ala Pro Met Lys 580 585 590 Ser Lys Pro Pro Pro Thr Tyr Glu Ser Glu Glu Glu Asp Lys Cys Lys 595 600 605 Pro Met Ser Tyr Glu Glu Lys Arg Gln Leu Ser Leu Asp Ile Asn Lys Leu Pro Gly Glu Lys Leu Gly Arg Val Val His Ile Ile Gln Ser Arg 625 630 635 Glu Pro Ser Leu Lys Asn Ser Asn Pro Asp Glu Ile Glu Ile Asp Phe $645 \ \ 650 \ \ 655$ Glu Thr Leu Lys Pro Ser Thr Leu Arg Glu Leu Glu Arg Tyr Val Thr 660 665 670 Ser Cys Leu Arg Lys Lys Arg Lys Pro Gln Ala Glu Lys Val Asp Val 675 680 685 Ile Ala Gly Ser Ser Lys Met Lys Gly Phe Ser Ser Ser Glu Ser Glu 690 695 700Ser Ser Ser Glu Ser Ser Ser Ser Asp Ser Glu Asp Ser Glu Thr Glu 705 710 720 Met Ala Pro Lys Ser Lys Lys Lys Gly His Pro Gly Arg Glu Gln Lys 725 730 735 Lys His His His His Gln Gln Met Gln Gln Ala Pro Ala Pro 740 750 Val Pro Gln Gln Pro Pro Pro Pro Pro Gln Gln Pro Pro Pro Pro Pro 755 760 765 Pro Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro Ser Met Pro Gln Gln Ala Ala Pro Ala Met Lys Ser Ser Pro Pro Pro Phe 785 790 795 800 Ile Ala Thr Gln Val Pro Val Leu Glu Pro Gln Leu Pro Gly Ser Val Phe Asp Pro Ile Gly His Phe Thr Gln Pro Ile Leu His Leu Pro Gln 820 830 Pro Glu Leu Pro Pro His Leu Pro Gln Pro Pro Glu His Ser Thr Pro Pro His Leu Asn Gln His Ala Val Val Ser Pro Pro Ala Leu His Asn 850 860

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Leu Pro Gln Gln Pro Ser Arg Pro Ser Asn Arg Ala Ala Ala Leu 865 870 875 880 Pro Pro Lys Pro Ala Arg Pro Pro Ala Val Ser Pro Ala Leu Thr Gln 885 890 895 Thr Pro Leu Leu Pro Gln Pro Pro Met Ala Gln Pro Pro Gln Val Leu Leu Glu Asp Glu Glu Pro Pro Ala Pro Pro Leu Thr Ser Met Gln Met Gln Leu Tyr Leu Gln Gln Leu Gln Lys Val Gln Pro Pro Thr Pro Leu 930 940 Leu Pro Ser Val Lys Val Gln Ser Gln Pro Pro Pro Pro Leu Pro 945 950 955 960 Pro Pro His Pro Ser Val Gln Gln Gln Leu Gln Gln Gln Pro Pro 965 970 975 Pro Pro Pro Gln Pro Gln Pro Pro Gln Gln His Gln Pro 980 985 990 Pro Pro Arg Pro Val His Leu Gln Pro Met Gln Phe Ser Thr His Ile 995 1000 1005 Gln Gln Pro Pro Pro Pro Gln Gly Gln Gln Pro Pro His Pro Pro 1010 1020 Pro Gly Gln Gln Pro Pro Pro Gln Pro Ala Lys Pro Gln Gln 1025 1030 1035 Val Ile Gln His His His Ser Pro Arg His His Lys Ser Asp Pro 1040 1050 Tyr Ser Thr Gly His Leu Arg Glu Ala Pro Ser Pro Leu Met Ile 1055 1065 His Ser Pro Gln Met Ser Gln Phe Gln Ser Leu Thr His Gln Ser 1070 1080 Pro Pro Gln Gln Asn Val Gln Pro Lys Lys Gln Glu Leu Arg Ala 1085 1090 1095 Ala Ser Val Val Gln Pro Gln Pro Leu Val Val Lys Glu Glu
1100 11105 1110 Lys Ile His Ser Pro Ile Ile Arg Ser Glu Pro Phe Ser Pro Ser 1115 1120 1125 Leu Arg Pro Glu Pro Pro Lys His Pro Glu Ser Ile Lys Ala Pro 1130 1140 Val His Leu Pro Gln Arg Pro Glu Met Lys Pro Val Asp Val Gly 1145 1150 1155 Arg Pro Val Ile Arg Pro Pro Glu Gln Asn Ala Pro Pro Pro Gly 1160 1170 Ala Pro Asp Lys Asp Lys Gln Lys Gln Glu Pro Lys Thr Pro Val

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ala Pro Lys Lys Asp Leu Lys Ile Lys Asn Met Gly Ser Trp Ala
1190 1195 1200

Ser Leu Val Gln Lys His Pro Thr Thr Pro Ser Ser Thr Ala Lys 1205 1215

Ser Ser Ser Asp Ser Phe Glu Gln Phe Arg Arg Ala Ala Arg Glu 1220 1230

Lys Glu Glu Arg Glu Lys Ala Leu Lys Ala Gln Ala Glu His Ala 1235 1240 1245

Glu Lys Glu Lys Glu Arg Leu Arg Gln Glu Arg Met Arg Ser Arg 1250 1260

Glu Asp Glu Asp Ala Leu Glu Gln Ala Arg Arg Ala His Glu Glu 1265 1270 1275

Ala Arg Arg Gln Glu Gln Gln Gln Gln Gln Arg Gln Glu Gln 1280 1285 1290

Gln Gln Gln Gln Gln Gln Ala Ala Ala Val Ala Ala Ala Ala Ala 1295 1300 1305

Thr Pro Gln Ala Gln Ser Ser Gln Pro Gln Ser Met Leu Asp Gln 1310 1320

Gln Arg Glu Leu Ala Arg Lys Arg Glu Gln Glu Arg Arg Arg 1325 1330 1335

Glu Ala Met Ala Ala Thr Ile Asp Met Asn Phe Gln Ser Asp Leu 1340 1350

Leu Ser Ile Phe Glu Glu Asn Leu Phe 1355

<210> 110

<211> 292

<213> Homo sapiens

<400> 110

Met Gln Lys Tyr Glu Lys Leu Glu Lys Ile Gly Glu Gly Thr Tyr Gly $10 ext{ } 15$

Thr Val Phe Lys Ala Lys Asn Arg Glu Thr His Glu Ile Val Ala Leu 20 25 30

Lys arg Val Arg Leu Asp Asp Asp Glu Gly Val Pro Ser Ser Ala 35 40 45

Leu Arg Glu Ile Cys Leu Leu Lys Glu Leu Lys His Lys Asn Ile Val 50 60

Arg Leu His Asp Val Leu His Ser Asp Lys Leu Thr Leu Val Phe 65 70 75 80

Glu Phe Cys Asp Gln Asp Leu Lys Lys Tyr Phe Asp Ser Cys Asn Gly 90 95

Asp Leu Asp Pro Glu Ile Val Lys Ser Phe Leu Phe Gln Leu Leu Lys

Gly Leu Gly Phe Cys His Ser Arg Asn Val Leu His Arg Asp Leu Lys

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Pro Glm Asn Leu Leu Ile Asn Arg Asn Gly Glu Leu Lys Leu Ala Asp

Phe Gly Leu Ala Arg Ala Phe Gly Ile Pro Val Arg Cys Tyr Ser Ala Glu Val Val Thr Leu Trp Tyr Arg Pro Pro Asp Val Leu Phe Gly Ala Lys Leu Tyr Ser Thr Ser Ile Asp Met Trp Ser Ala Gly Cys Ile Phe Ala Glu Leu Leu Ala Asn Ala Gly Arg Pro Leu Phe Pro Gly Asn Asp Val Asp Asp Gln Leu Lys Arg Ile Phe Arg Leu Leu Gly Thr Pro Thr Glu Met Tyr Pro Ala Thr Ser Leu Val Asp Val Asp Val Val Pro Lys Leu Asn Ala Thr Gly Arg Asp Leu Leu Gln Asp Leu Leu Lys Cys Asp Pro Val Gln Arg Ile Ser Ala Glu Glu Glu Ala Leu Gln His Pro Tyr Phe Ser Asp Phe Cys Pro Pro

<210> 111 <211> 765

<211> 765

<213> Homo sapiens

<400> 111

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Asp Tyr Lys Pro Lys Lys Ile Lys Thr Glu Asp Thr Lys Lys Glu
145 150 160 Lys Lys Arg Lys Leu Glu Glu Glu Glu Asp Gly Lys Leu Lys Lys Pro Lys Asn Lys Asp Lys Asp Lys Lys Val Pro Glu Pro Asp Asn Lys Lys 180 185 190 Lys Lys Pro Lys Lys Glu Glu Glu Gln Lys Trp Lys Trp Trp Glu Glu .195 200 205 Glu Arg Tyr Pro Glu Gly Ile Lys Trp Lys Phe Leu Glu His Lys Gly 210 220 Pro Val Phe Ala Pro Pro Tyr Glu Pro Leu Pro Glu Asn Val Lys Phe 225 230 235 240 Tyr Tyr Asp Gly Lys Val Met Lys Leu Ser Pro Lys Ala Glu Glu Val 245 250 255 Ala Thr Phe Phe Ala Lys Met Leu Asp His Glu Tyr Thr Thr Lys Glu 260 265 270 Ile Phe Arg Lys Asn Phe Phe Lys Asp Trp Arg Lys Glu Met Thr Asn 275 280 285 Glu Glu Lys Asn Ile Ile Thr Asn Leu Ser Lys Cys Asp Phe Thr Gln 290 295 300 Met Ser Gln Tyr Phe Lys Ala Gln Thr Glu Ala Arg Lys Gln Met Ser 305 310 315 Lys Glu Glu Lys Leu Lys Ile Lys Glu Glu Asn Glu Lys Leu Lys 335 Glu Tyr Gly Phe Cys Ile Met Asp Asn His Lys Glu Arg Ile Ala Asn 340 345 Phe Lys Ile Glu Pro Pro Gly Leu Phe Arg Gly Arg Gly Asn His Pro 355 365Lys Met Gly Met Leu Lys Arg Arg Ile Met Pro Glu Asp Ile Ile Ile 370 380 Asn Cys Ser Lys Asp Ala Lys Val Pro Ser Pro Pro Pro Gly His Lys 385 390 400 Trp Lys Glu Val Arg His Asp Asn Lys Val Thr Trp Leu Val Ser Trp 405 410 415Thr Glu Asn Ile Gln Gly Ser Ile Lys Tyr Ile Met Leu Asn Pro Ser

Ser Arg Ile Lys Gly Glu Lys Asp Trp Gln Lys Tyr Glu Thr Ala Arg 435 440 445

Arg Leu Lys Lys Cys Val Asp Lys Ile Arg Asn Gln Tyr Arg Glu Asp

Trp Lys Ser Lys Glu Met Lys Val Arg Gln Arg Ala Val Ala Leu Tyr

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Phe Ile Asp Lys Leu Ala Leu Arg Ala Gly Asn Glu Lys Glu Gly
485
490
495

Glu Thr Ala Asp Thr Val Gly Cys Cys Ser Leu Arg Val Glu His Ile 500 505 510 Asn Leu His Pro Glu Leu Asp Gly Gln Glu Tyr Val Val Glu Phe Asp 515 520 525 Phe Leu Gly Lys Asp Ser Ile Arg Tyr Tyr Asn Lys Val Pro Val Glu 530 540 Lys Arg Val Phe Lys Asn Leu Gln Leu Phe Met Glu Asn Lys Gln Pro Glu Asp Asp Leu Phe Asp Arg Leu Asn Thr Gly Ile Leu Asn Lys His 565 570 575 Leu Gln Asp Leu Met Glu Gly Leu Thr Ala Lys Val Phe Arg Thr Tyr 580 585 590 Asn Ala Ser Ile Thr Leu Gln Gln Gln Leu Lys Glu Leu Thr Ala Pro 595 600 605 ASP Glu ASP Ile Pro Ala Lys Ile Leu Ser Tyr ASP Arg Ala ASP Arg 610 620 Ala Val Ala Ile Leu Cys Asn His Gln Arg Ala Pro Pro Lys Thr Phe 625 630 635 640 Glu Lys Ser Met Met Asn Leu Gln Thr Lys Ile Asp Ala Lys Lys Glu
645 650 655 Gln Leu Ala Asp Ala Arg Arg Asp Leu Lys Ser Ala Lys Ala Asp Ala 660 665 670 Lys Val Met Lys Asp Ala Lys Thr Lys Lys Val Val Glu Ser Lys Lys 675 680 685 Lys Ala Val Gln Arg Leu Glu Glu Gln Leu Met Lys Leu Glu Val Gln
690 695 700 Ala Thr Asp Arg Glu Glu Asn Lys Gln Ile Ala Leu Gly Thr Ser Lys 705 710 715 720 Leu Asn Tyr Leu Asp Pro Arg Ile Thr Val Ala Trp Cys Lys Lys Trp
725 730 735 Gly Val Pro Ile Glu Lys Ile Tyr Asn Lys Thr Gln Arg Glu Lys Phe 740 745 750 Ala Trp Ala Ile Asp Met Ala Asp Glu Asp Tyr Glu Phe

<210> 112 <211> 691 <212> PRT

<213> Homo sapiens

<400> 112

Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile 1 10 15

Lys Met Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly 20 25 30

Protein Complexes of cellular networks underlying the development of cancer and other diseases.sT25.txt

Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys

35
40

Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr Ala ASN Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly 90 95 Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg 100 105 110 Leu Tyr Ser Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala 115 120 125 Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val 130 135 140 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala 145 150 155 160Gly Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val 165 170 175 Gly Trp Lys Lys Leu Lys Glu Val Phe Ser Met Ala Gly Val Val Val 180 185 190 Arg Ala Asp Ile Leu Glu Asp Lys Asp Gly Lys Ser Arg Gly Ile Gly 195 200 205Thr Val Thr Phe Glu Gln Ser Ile Glu Ala Val Gln Ala Ile Ser Met 210 215 220 Phe Asn Gly Gln Leu Leu Phe Asp Arg Pro Met His Val Lys Met Asp 225 230 235 240 Glu Arg Ala Leu Pro Lys Gly Asp Phe Phe Pro Pro Glu Arg Pro Gln 245 250 255 Gln Leu Pro His Gly Leu Gly Gly Ile Gly Met Gly Leu Gly Pro Gly 260 265 270 Gly Gln Pro Ile Asp Ala Asn His Leu Asn Lys Gly Ile Gly Met Gly 275 280 285 Asn Ile Gly Pro Ala Gly Met Gly Met Glu Gly Ile Gly Phe Gly Ile Asn Lys Met Gly Gly Met Glu Gly Pro Phe Gly Gly Gly Met Glu Asn 305 310 315 320 Met Gly Arg Phe Gly Ser Gly Met Asn Met Gly Arg Ile Asn Glu Ile 325 330 335 Leu Ser Asn Ala Leu Lys Arg Gly Glu Ile Ile Ala Lys Gln Gly Gly Gly Gly Gly Gly Ser Val Pro Gly Ile Glu Arg Met Gly Pro Gly 355 360 365 Ile Asp Arg Leu Gly Gly Ala Gly Met Glu Arg Met Gly Ala Gly Leu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 370 375

Gly His Gly Met Asp Arg Val Gly Ser Glu Ile Glu Arg Met Gly Leu 385 390 395 400 Val Met Asp Arg Met Gly Ser Val Glu Arg Met Gly Ser Gly Ile Glu
405 410 415 Arg Met Gly Pro Leu Gly Leu Asp His Met Ala Ser Ser Ile Glu Arg 420 425 430 Met Gly Gln Thr Met Glu Arg Ile Gly Ser Gly Val Glu Arg Met Gly 435 440 445 Ala Gly Met Gly Phe Gly Leu Glu Arg Met Ala Ala Pro Ile Asp Arg 450 455 460 Val Gly Gln Thr Ile Glu Arg Met Gly Ser Gly Val Glu Arg Met Gly 465 470 475 480 Pro Ala Ile Glu Arg Met Gly Leu Ser Met Glu Arg Met Val Pro Ala 485 490 495 Gly Met Gly Ala Gly Leu Glu Arg Met Gly Pro Val Met Asp Arg Met 500 505 510 Ala Thr Gly Leu Glu Arg Met Gly Ala Asn Asn Leu Glu Arg Met Gly 515 525 Leu Glu Arg Met Gly Ala Asn Ser Leu Glu Arg Met Gly Leu Glu Arg 530 540 Met Gly Ala Asn Ser Leu Glu Arg Met Gly Pro Ala Met Gly Pro Ala 545 550 560 Leu Gly Ala Gly Ile Glu Arg Met Gly Leu Ala Met Gly Gly Gly Gly 575 Gly Ala Ser Phe Asp Arg Ala Ile Glu Met Glu Arg Gly Asn Phe Gly 580 585 590 Gly Ser Phe Ala Gly Ser Phe Gly Gly Ala Gly Gly His Ala Pro Gly 595 600 605 Val Ala Arg Lys Ala Cys Gln Ile Phe Val Arg Asn Leu Pro Phe Asp 610 615 620 Phe Thr Trp Lys Met Leu Lys Asp Lys Phe Asn Glu Cys Gly His Val 625 630 635 640 Leu Tyr Ala Asp Ile Lys Met Glu Asn Gly Lys Ser Lys Gly Cys Gly 655 655 Val Val Lys Phe Glu Ser Pro Glu Val Ala Glu Arg Ala Cys Arg Met Met Asn Gly Met Lys Leu Ser Gly Arg Glu Ile Asp Val Arg Ile Asp Arg Asn Ala 690

<210> 113

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <213> Homo sapiens

<400> 113

Met Ala Pro Ser Arg Asn Gly Met Val Leu Lys Pro His Phe His Lys 1 10

Asp Trp Gln Arg Arg Val Ala Thr Trp Phe Asn Gln Pro Ala Arg Lys

Ile Arg Arg Lys Ala Arg Gln Ala Lys Ala Arg Arg Ile Ala Pro 35 40 45

Arg Pro Ala Ser Gly Pro Ile Arg Pro Ile Val Arg Cys Pro Thr Val 50 60

Arg Tyr His Thr Lys Val Arg Ala Gly Arg Gly Phe Ser Leu Glu Glu 65 70 75

Leu Arg Val Ala Gly Ile His Lys Lys Val Ala Arg Thr Ile Gly Ile

Ser Val Asp Pro Arg Arg Arg Asn Lys Ser Thr Glu Ser Leu Gln Ala $100 \hspace{1cm} 105 \hspace{1cm} 110$

Asn Val Gln Arg Leu Lys Glu Tyr Arg Ser Lys Leu Ile Leu Phe Pro 115 120 125

Arg Lys Pro Ser Ala Pro Lys Lys Gly Asp Ser Ser Ala Glu Glu Leu 130 140

Lys Leu Ala Thr Gln Leu Thr Gly Pro Val Met Pro Val Arg Asn Val 145 150 160

Tyr Lys Lys Glu Lys Ala Arg Val Ile Thr Glu Glu Lys Asn Phe $165 \hspace{0.5cm} 170 \hspace{0.5cm} 175$

Lys Ala Phe Ala Ser Leu Arg Met Ala Arg Ala Asn Ala Arg Leu Phe 180 185 190

Gly Ile Arg Ala Lys Arg Ala Lys Glu Ala Ala Glu Gln Asp Val Glu 195 200 205

Lys Lys Lys

<210> 114 <211> 605 <212> PRT

<212> PK1 <213> Homo sapiens

<400> 114

Met Phe Val Cys Ile Asp Asp Leu Gly Asp Ser Val Val Leu Pro Gly

Arg Gln Gln His Gly Arg Met Ala Ala Ile Leu Ile Leu Gln 20 30

Leu Thr Phe Leu Lys Met Thr Ser Gly Asp Glu Val His Gly Thr Ser 35 40 45

Ser Ile Leu Lys His Thr Ser Val Pro Gly Lys His Gln Asp Ser Leu 50 60

Tyr Thr Leu Thr Arg Cys Pro Val Val Met Glu Thr Arg Ile Leu Thr 65 70 75

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Thr Lys Asp Leu Glu Gly Val Arg Gly Cys Arg Leu Ala Gly Pro Ala

95

Val Gly Lys Pro Gly Glu Arg Tyr Pro Pro Ile Gly Thr Phe Tyr 100 105 110 Cys Val Leu Lys Gly Val Gln Gly Pro Gly Ser Val Phe Asp Ile Val Ala Asn Ser His Lys Tyr Pro Glu His Leu Ile Pro Ser Lys Met Gly $130 \hspace{1cm} 135 \hspace{1cm} 140$ Leu Ser Pro Ala Cys Leu Pro Ser Ser Tyr Asp Pro Gly Lys Asp Cys 145 150 155 160 Ser Gly Arg Cys Pro Leu Cys Gly Trp Glu Ala Ser Glu Ala Arg Leu 165 170 175Gln Ala His Gln Arg Val Cys Gly Arg Gly His Val Ala Ala Ile Phe 180 185 190 Cys Leu Leu Val Ser Val Cys Arg His Pro Met Glu Asp Ser Met Asp Met His Met Ser Pro Leu Arg Pro Gln Asn Tyr Leu Phe Ser Cys Glu 210 220 220 Leu Lys Ala Asn Lys Asp Asp His Phe Lys Val Asp Asn Asp Glu Asn 225 230 235 Glu His Gln Leu Ser Leu Arg Thr Cys Gly Ser Gly Pro Val His Ile 245 250 255 Ser Gly Gln His Leu Val Ala Val Glu Glu Asp Ala Glu Ser Glu Asp 260 270 Glu Glu Glu Ser Ala Lys Leu Leu Ser Ile Ser Gly Lys Gln Ser 275 280 285 Val Pro Gly Gly Gly Ser Lys Val Pro Gln Lys Gln Asp Cys Arg Asp 290 295 300 Ser Pro Arg Gly Ala Thr Ser Asp Glu Leu Gly Lys Ala Leu Gly Trp 305 310 315 .320 Val Arg Ala Gly Gln Arg Pro Pro Ile Lys Glu Trp Gly Ser Gly Met Glu Ala Gly Ser Val Gly Glu Pro Gly Gly Ala Ala Gly Ser Ser Gln Gln val Glu Glu Thr Pro Tyr Leu Ser Met Gly Ala Asp Cys Gln Glu 355 360 365 Arg Gln Glu Phe Cys Glu Leu Ala Ser Val Arg Val Ala Ser Ser Ala Cys Ile Gly Ser Ser Gly Asp Val Ser Ser Leu Pro Pro Ser Phe Val Lys His Lys Phe Gln Asp Asn Ile Ile Asn Thr Phe Lys Thr Ala Ala
405
410
415 Ala Glu His Gln Thr Arg Ser Val Gln Ala Pro Lys Cys Ala Ala Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 420 425 430 Glu Ala Ala Leu Arg Pro Gly Ser Pro Val Ala Thr Gly Pro Leu His
435 440 445 Trp Glu Thr Asp Leu Gly Leu Arg Asn Leu Arg Thr Gln Met Ser Ser 450 455 460 Pro Leu Gln Trp Ser Gln Ser Arg Tyr Ser Gln Val Arg Gly Cys Ser 465 470 475 480 Gln Ala Leu Ser Asp Ser Thr Val Ile Gln Glu Lys His His Thr Ser 485 490 495 Val Pro Ser Thr Val Gly His Tyr Asn Arg Arg Gly Lys Ala Arg Val 500 505 510 Gln Thr Pro Pro Arg Thr Pro Ser Arg Pro Pro Ser Ala Gly Ala Pro 515 520 525 Glu Arg His Ala Pro Arg Gly Ser Pro Ala Pro Ser Arg Pro Gln Ser 530 540 Ala Ala Glu Arg Asn Gly Asn Trp Ala Asp Ala Arg Arg Arg Leu Thr 545 550 555 Ile Arg Ala Ala Arg Arg Leu Thr Ser Pro Cys Val Asp Gln Pro Pro 575 570 575 Glu Pro Gly Lys Arg Arg Ser Leu Ile Gly Cys Ala Gly Gly Leu
580 585 590 Gly Ala Asn Asp Arg Ala Ala Ser Gly Gly Val Trp Pro 595 600

Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser 1 10 15 Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His 50 55 Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser 115 120 125

<210> 115 <211> 579 <212> PRT

Homo sapiens

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu 130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala 145 150 155 160 Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Gly Leu Gly Gln 165 170 175 Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
185 190 Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
210 215 220 Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala 225 230 235 240 Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala 245 250 255 Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys 260 265 270 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val 275 280 285 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu 305 310 315 320 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu 340 345 350 Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu 355 360 365 Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro 370 380 Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe 385 390 . 395 400 Glu Gln Ser Glu Thr Glu Thr Val His Gln Phe Ile Pro Ala Leu Ser Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe 450 460 Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val 470 475 Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser 485 490 495 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu Leu Gln Asn Leu Ser Ser Ala Glu Val Val Pro Arg Asp Gln Thr 515 520 525 Pro Asp Glu Asn Asp Gln Val Val Lys Ile Thr Gly His Phe Tyr 530 540 Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val 545 550 555 560 Lys Gln His Gln Gln Eys Ala Leu Gln Ser Gly Pro Pro Gln Ser 565 570 575

Arg Arg Lys

116 1328 PRT Homo sapiens

<400> 116

Met Glu Ser Arg Asp Pro Ala Gln Pro Met Ser Pro Gly Glu Ala Thr 1 10 15 Gln Ser Gly Ala Arg Pro Ala Asp Arg Tyr Gly Leu Leu Lys His Ser 20 30 Arg Glu Phe Leu Asp Phe Phe Trp Asp Ile Ala Lys Pro Glu Gln Glu 35 40 45 Thr Arg Leu Ala Ala Thr Glu Lys Leu Leu Glu Tyr Leu Arg Gly Arg 50 60 Pro Lys Gly Ser Glu Met Lys Tyr Ala Leu Lys Arg Leu Ile Thr Gly 65 70 75 80 Leu Gly Val Gly Arg Glu Thr Ala Arg Pro Cys Tyr Ser Leu Ala Leu 85 90 95 Ala Gln Leu Cu Gln Ser Phe Glu Asp Leu Pro Leu Cys Ser Ile Leu 100 105 110 Gln Gln Ile Gln Glu Lys Tyr Asp Leu His Gln Val Lys Lys Ala Met Leu Arg Pro Ala Leu Phe Ala Asn Leu Phe Gly Val Leu Ala Leu Phe 130 135 140 Gln Ser Gly Arg Leu Val Lys Asp Gln Glu Ala Leu Met Lys Ser Val 145 150 155 160 Lys Leu Leu Gln Ala Leu Ala Gln Tyr Gln Asn His Leu Gln Glu Gln 165 170 175 Pro Arg Lys Ala Leu Val Asp Ile Leu Ser Glu Val Ser Lys Ala Thr

Leu Gln Glu Ile Leu Pro Glu Val Leu Lys Ala Asp Leu Asn Ile Ile

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 195 200 205

Leu Ser Ser Pro Glu Gln Leu Glu Leu Phe Leu Leu Ala Gln Gln Lys 210 220 val Pro Ser Lys Leu Lys Lys Leu Val Gly Ser Val Asn Leu Phe Ser 225 230 235 240 Asp Glu Asn Val Pro Arg Leu Val Asn Val Leu Lys Met Ala Ala Ser 255 Ser Val Lys Lys Asp Arg Lys Leu Pro Ala Ile Ala Leu Asp Leu Leu 260 265 270Arg Leu Ala Leu Lys Glu Asp Lys Phe Pro Arg Phe Trp Lys Glu Val 275 280 285 Val Glu Gln Gly Leu Leu Lys Met Gln Phe Trp Pro Ala Ser Tyr Leu 290 295 300 Cys Phe His Leu Leu Gly Ala Ala Leu Pro Leu Leu Thr Lys Glu Gln 305 310 315 320 Leu His Leu Val Met Gln Gly Asp Val Ile Arg His Tyr Gly Glu His 325 330 335 Val Cys Thr Ala Lys Leu Pro Lys Gln Phe Lys Phe Ala Pro Glu Met 340 345Asp Asp Tyr Val Gly Thr Phe Leu Glu Gly Cys Gln Asp Asp Pro Glu Arg Gln Leu Ala Val Leu Val Ala Phe Ser Ser Val Thr Asn Gln Gly Leu Pro Val Thr Pro Thr Phe Trp Arg Val Val Arg Phe Leu Ser Pro 385 390 395 Pro Ala Leu Gln Gly Tyr Val Ala Trp Leu Arg Ala Met Phe Leu Gln 405 410 415 Pro Asp Leu Asp Ser Leu Val Asp Phe Ser Thr Asn Asn Gln Lys Lys Ala Gln Asp Ser Ser Leu His Met Pro Glu Arg Ala Val Phe Arg Leu 435 440 445 Arg Lys Trp Ile Ile Phe Arg Leu Val Ser Ile Val Asp Ser Leu His Leu Glu Met Glu Glu Ala Leu Thr Glu Gln Val Ala Arg Phe Cys Leu 465 470 475 Phe His Ser Phe Phe Val Thr Lys Lys Pro Thr Ser Gln Ile Pro Glu
485 490 495 Thr Lys His Pro Phe Ser Phe Pro Leu Glu Asn Gln Ala Arg Glu Ala 500 505 510 Val Ser Ser Ala Phe Phe Ser Leu Leu Gln Thr Leu Ser Thr Gln Phe 515 520 525 Lys Gln Ala Pro Gly Gln Thr Gln Gly Gln Pro Trp Thr Tyr His



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Val Gln Phe Ala Asp Leu Leu Leu Asn His Ser His Asn Val Thr Thr Val Thr Pro Phe Thr Ala Gln Gln His Gln Ala Trp Asp Arg Met 565 570 575 Leu Gln Thr Leu Lys Glu Leu Glu Ala His Ser Ala Glu Ala Arg Ala 580 585 590 Ala Ala Phe Gln His Leu Leu Leu Phe Val Gly Ile His Leu Leu Lys 595 600 605 Ser Pro Ala Glu Ser Cys Asp Leu Leu Gly Asp Ile Gln Thr Cys Ile 610 620Arg Lys Ser Leu Gly Glu Lys Pro Arg Arg Ser Arg Thr Lys Thr Ile 625 630 635 640 Asp Pro Gln Glu Pro Pro Trp Val Glu Val Leu Val Glu Ile Leu Leu 645 650 655 Ala Leu Leu Ala Gln Pro Ser His Leu Met Arg Gln Val Ala Arg Ser 660 665 670 Val Phe Gly His Ile Cys Ser His Leu Thr Pro Arg Ala Leu Gln Leu 675 680 685 Ile Leu Asp Val Leu Asn Pro Glu Thr Ser Glu Asp Glu Asn Asp Arg Val Val Val Thr Asp Asp Ser Asp Glu Arg Arg Leu Lys Gly Ala Glu 705 710 715 720 Asp Lys Ser Glu Glu Gly Glu Asp Asn Arg Ser Ser Glu Ser Glu Glu 725 730 735 Glu Ser Glu Gly Glu Glu Glu Glu Glu Glu Arg Asp Gly Asp Val 740 745 Asp Gln Gly Phe Arg Glu Gln Leu Met Thr Val Leu Gln Ala Gly Lys 755 760 765 Ala Leu Gly Glu Asp Ser Glu Asn Glu Glu Leu Gly Asp Glu 770 780 Ala Met Met Ala Leu Asp Gln Ser Leu Ala Ser Leu Phe Ala Glu Gln 785 790 795 800 Lys Leu Arg Ile Gln Ala Arg Arg Asp Glu Lys Asn Lys Leu Gln Lys 805 810 815 Glu Lys Ala Leu Arg Arg Asp Phe Gln Ile Arg Val Leu Asp Leu Val 820 825 830 Glu Val Leu Val Thr Lys Gln Pro Glu Asn Ala Leu Val Leu Glu Leu 835 840 845 Leu Glu Pro Leu Leu Ser Ile Ile Arg Arg Ser Leu Arg Ser Ser Ser 850 855 Ser Lys Gln Glu Gln Asp Leu Leu His Lys Thr Ala Arg Ile Phe Thr 865 870 875 880 His His Leu Cys Arg Ala Arg Arg Tyr Cys His Asp Leu Gly Glu Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 885 890 895

Ala Gly Ala Leu His Ala Gln Val Glu Arg Leu Val Gln Gln Ala Gly 900 905 910

Arg Gln Pro Asp Ser Pro Thr Ala Leu Tyr His Phe Asn Ala Ser Leu 915 920 925

Tyr Leu Leu Arg Val Leu Lys Gly Asn Thr Ala Glu Gly Cys Val His

Glu Thr Gln Glu Lys Gln Lys Ala Gly Thr Asp Pro Ser His Met Pro 945 950 955 960

Thr Gly Pro Gln Ala Ala Ser Cys Leu Asp Leu Asn Leu Val Thr Arg 965 970 975

Val Tyr Ser Thr Ala Leu Ser Ser Phe Leu Thr Lys Arg Asn Ser Pro 980 985 990

Leu Thr Val Pro Met Phe Leu Ser Leu Phe Ser Arg His Pro Val Leu 995 1000 1005

Cys Gln Ser Leu Leu Pro Ile Leu Val Gln His Ile Thr Gly Pro $1010 \hspace{1cm} 1020$

Val Arg Pro Arg His Gln Ala Cys Leu Leu Leu Gln Lys Thr Leu 1025 1030 1035

Ser Met Arg Glu Val Arg Ser Cys Phe Glu Asp Pro Glu Trp Lys 1040 1045 1050

Gln Leu Met Gly Gln Val Leu Ala Lys Val Thr Glu Asn Leu Arg 1055 1060 1065

Val Leu Gly Glu Ala Gln Thr Lys Ala Gln His Gln Gln Ala Leu 1070 1075 1080

Ser Ser Leu Glu Leu Leu Asn Val Leu Phe Arg Thr Cys Lys His 1085 1095

Glu Lys Leu Thr Leu Asp Leu Thr Val Leu Leu Gly Val Leu Gln 1100 1105

Gly Gln Gln Gln Ser Leu Gln Gln Gly Ala His Ser Thr Gly Ser 1125 1120 1125

Ser Arg Leu His Asp Leu Tyr Trp Gln Ala Met Lys Thr Leu Gly 1130 1140

Val Gln Arg Pro Lys Leu Glu Lys Lys Asp Ala Lys Glu Ile Pro 1145 1150 1155

Ser Ala Thr Gln Ser Pro Ile Ser Lys Lys Arg Lys Lys Gly 1160 1165 1170

Phe Leu Pro Glu Thr Lys Lys Arg Lys Arg Lys Ser Glu Asp 1175 1180 1185

Gly Thr Pro Ala Glu Asp Gly Thr Pro Ala Ala Thr Gly Gly Ser 1190 1195 1200

Gln Pro Pro Ser Met Gly Arg Lys Lys Arg Asn Arg Thr Lys Ala 1205 1210 1215 WO 2004/009622 PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Lys Val Pro Ala Gln Ala Asn Gly Thr Pro Thr Thr Lys Ser Pro 1220 1230

Ala Pro Gly Ala Pro Thr Arg Ser Pro Ser Thr Pro Ala Lys Ser

Pro Lys Leu Gln Lys Lys Asn Gln Lys Pro Ser Gln Val Asn Gly 1250 1260

Ala Pro Gly Ser Pro Thr Glu Pro Ala Gly Gln Lys Gln His Gln 1265 1270 1275

Lys Ala Leu Pro Lys Lys Gly Val Leu Gly Lys Ser Pro Leu Ser 1280 1285 1290

Ala Leu Ala Arg Lys Lys Ala Arg Leu Ser Leu Val Ile Arg Ser 1295 1300 1305

Pro Ser Leu Leu Gln Ser Gly Ala Lys Lys Lys Ala Gln Val Arg 1310 1320

Lys Ala Gly Lys Pro

117 504 PRT

Homo sapiens

<400> 117

Met Ser Leu Ile Cys Ser Ile Ser Asn Glu Val Pro Glu His Pro Cys $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Val Ser Pro Val Ser Asn His Val Tyr Glu Arg Arg Leu Ile Glu Lys

Tyr Ile Ala Glu Asn Gly Thr Asp Pro Ile Asn Asn Gln Pro Leu Ser

Glu Glu Gln Leu Ile Asp Ile Lys Val Ala His Pro Ile Arg Pro Lys

Pro Pro Ser Ala Thr Ser Ile Pro Ala Ile Leu Lys Ala Leu Gln Asp

Glu Trp Asp Ala Val Met Leu His Ser Phe Thr Leu Arg Gln Gln Leu 85 90 95

Gln Thr Thr Arg Gln Glu Leu Ser His Ala Leu Tyr Gln His Asp Ala 100 105 110

Ala Cys Arg Val Ile Ala Arg Leu Thr Lys Glu Val Thr Ala Ala Arg

Glu Ala Leu Ala Thr Leu Lys Pro Gln Ala Gly Leu Ile Val Pro Gln

Ala val Pro Ser Ser Gln Pro Ser Val Val Gly Ala Gly Glu Pro Met

Asp Leu Gly Glu Leu Val Gly Met Thr Pro Glu Ile Ile Gln Lys Leu $165 \hspace{1cm} 170 \hspace{1cm} 175$

Gln Asp Lys Ala Thr Val Leu Thr Thr Glu Arg Lys Lys Arg Gly Lys 180 185 190



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Val Pro Glu Glu Leu Val Lys Pro Glu Glu Leu Ser Lys Tyr Arg Gln Val Ala Ser His Val Gly Leu His Ser Ala Ser Ile Pro Gly Ile Leu Ala Leu Asp Leu Cys Pro Ser Asp Thr Asn Lys Ile Leu Thr Gly 225 230 240 Gly Ala Asp Lys Asn Val Val Phe Asp Lys Ser Ser Glu Gln Ile 245 250 255 Leu Ala Thr Leu Lys Gly His Thr Lys Lys Val Thr Ser Val Val Phe 260 265 270 His Pro Ser Gln Asp Leu Val Phe Ser Ala Ser Pro Asp Ala Thr Ile 275 280 285 Arg Ile Trp Ser Val Pro Asn Ala Ser Cys Val Gln Val Val Arg Ala 290 295 300 His Glu Ser Ala Val Thr Gly Leu Ser Leu His Ala Thr Gly Asp Tyr 305 310 315 320 Leu Leu Ser Ser Ser Asp Asp Gln Tyr Trp Ala Phe Ser Asp Ile Gln 325 330 335 Thr Gly Arg Val Leu Thr Lys Val Thr Asp Glu Thr Ser Gly Cys Ser 340 345Leu Thr Cys Ala Gln Phe His Pro Asp Gly Leu Ile Phe Gly Thr Gly 355 360 365 Thr Met Asp Ser Gln Ile Lys Ile Trp Asp Leu Lys Glu Arg Thr Asn $\frac{370}{370}$ Val Ala Asn Phe Pro Gly His Ser Gly Pro Ile Thr Ser Ile Ala Phe 385 390 395 400 Ser Glu Asn Gly Tyr Tyr Leu Ala Thr Ala Ala Asp Asp Ser Ser Val 405 410 415 Lys Leu Trp Asp Leu Arg Lys Leu Lys Asn Phe Lys Thr Leu Gln Leu Asp Asn Asn Phe Glu Val Lys Ser Leu Ile Phe Asp Gln Ser Gly Thr 435 440 445Tyr Leu Ala Leu Gly Gly Thr Asp Val Gln Ile Tyr Ile Cys Lys Gln 450 460 Trp Thr Glu Ile Leu His Phe Thr Glu His Ser Gly Leu Thr Thr Gly 465 470 475 Val Ala Phe Gly His His Ala Lys Phe Ile Ala Ser Thr Gly Met Asp 485 490 495 Arg Ser Leu Lys Phe Tyr Ser Leu

<210> 118 <211> 596

<212> PRT <213> Homo sapiens



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <400> 118

Met Val Leu Leu His Val Leu Phe Glu His Ala Val Gly Tyr Ala Leu 1 10 15 Val Ala Leu Lys Glu Val Glu Glu Ile Ser Leu Leu Gln Pro Gln Val 20 25 30 Glu Glu Ser Val Leu Asn Leu Gly Lys Phe His Ser Ile Val Arg Leu 35 40 45 Val Ala Phe Cys Pro Phe Ala Ser Ser Gln Val Ala Leu Glu Asn Ala 50 55 60 Asn Ala Val Ser Glu Gly Val Val His Glu Asp Leu Arg Leu Leu Leu 65 70 80 Glu Thr His Leu Pro Ser Lys Lys Lys Val Leu Leu Gly Val Gly
85 90 95 Asp Pro Lys Ile Gly Ala Ala Ile Gln Glu Glu Leu Gly Tyr Asn Cys 100 105 110 Gln Thr Gly Gly Val Ile Ala Glu Ile Leu Arg Gly Val Arg Leu His 115 120 125 Phe His Asn Leu Val Lys Gly Leu Thr Asp Leu Ser Ala Cys Lys Ala Gln Leu Gly Leu Gly His Ser Tyr Ser Arg Ala Lys Val Lys Phe Asn 145 150 155 160 Val Asn Arg Val Asp Asn Met Ile Ile Gln Ser Ile Ser Leu Leu Asp 165 170 175 Gln Leu Asp Lys Asp Ile Asn Thr Phe Ser Met Arg Val Arg Glu Trp 180 185 190 Tyr Gly Tyr His Phe Pro Glu Leu Val Lys Ile Ile Asn Asp Asn Ala 195 200 205Thr Tyr Cys Arg Leu Ala Gln Phe Ile Gly Asn Arg Arg Glu Leu Asn 210 225 Glu Asp Lys Leu Glu Lys Leu Glu Glu Leu Thr Met Asp Gly Ala Lys 225 230 235 240 Ala Lys Ala Ile Leu Asp Ala Ser Arg Ser Ser Met Gly Met Asp Ile 245 250 255 Ser Ala Ile Asp Leu Ile Asn Ile Glu Ser Phe Ser Ser Arg Val Val Ser Leu Ser Glu Tyr Arg Gln Ser Leu His Thr Tyr Leu Arg Ser Lys 275 280 285 Met Ser Gln Val Ala Pro Ser Leu Ser Ala Leu Ile Gly Glu Ala Val 290 295 300 Gly Ala Arg Leu Ile Ala His Ala Gly Ser Leu Thr Asn Leu Ala Lys 305 310 315 320 Tyr Pro Ala Ser Thr Val Gln Ile Leu Gly Ala Glu Lys Ala Leu Phe

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Ala Leu Lys Thr Arg Gly Asn Thr Pro Lys Tyr Gly Leu Ile Phe His Ser Thr Phe Ile Gly Arg Ala Ala Lys Asn Lys Gly Arg Ile Ser Arg Tyr Leu Ala Asn Lys Cys Ser Ile Ala Ser Arg Ile Asp Cys 370 380 Phe Ser Glu Val Pro Thr Ser Val Phe Gly Glu Lys Leu Arg Glu Gln 385 390 395 400 Val Glu Glu Arg Leu Ser Phe Tyr Glu Thr Gly Glu Ile Pro Arg Lys 405 410 415 Asn Leu Asp Val Met Lys Glu Ala Met Val Gln Ala Glu Ala Glu Glu 420 425 430 Ala Ala Glu Ile Thr Arg Lys Leu Glu Lys Gln Glu Lys Lys Arg Leu Lys Lys Glu Lys Lys Arg Leu Ala Ala Leu Ala Leu Ala Ser Ser 450 460Glu Asn Ser Ser Ser Thr Pro Glu Glu Cys Glu Glu Met Ser Glu Lys
465 470 475 480 Pro Lys Lys Lys Lys Gln Lys Pro Gln Glu Val Pro Gln Glu Asn 485 490 495 Gly Met Glu Asp Pro Ser Ile Ser Phe Ser Lys Pro Lys Lys Lys 500 505 510 Ser Phe Ser Lys Glu Glu Leu Met Ser Ser Asp Leu Glu Glu Thr Ala 515 520 525 Gly Ser Thr Ser Ile Pro Lys Arg Lys Lys Ser Thr Pro Lys Glu Glu 530 540 Thr Val Asn Asp Pro Glu Glu Ala Gly His Arg Ser Gly Ser Lys Lys 545 555 560 Lys Arg Lys Phe Ser Lys Glu Glu Pro Val Ser Ser Gly Pro Glu Glu 575 Ala Val Gly Lys Ser Ser Ser Lys Lys Lys Lys Phe His Lys Ala Ser Gln Glu Asp

<210> 119 <211> 715

<213> Homo sapiens

<400> 119

Met Asn Ser Pro Lys Ser Lys Lys Ala Lys Lys Lys Glu Glu Pro Ser 1 10 15 Ser Gln Asn Asp Ile Ser Pro Lys Thr Lys Ser Leu Arg Lys Lys Lys Glu Pro Ile Glu Lys Lys Val Val Ser Ser Lys Thr Lys Lys Val Thr Lys 45

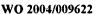
Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asn Glu Glu Pro Ser Glu Glu Glu Ile Asp Ala Pro Lys Pro Lys Lys Met Lys Lys Glu Lys Glu Met Asn Gly Glu Thr Arg Glu Lys Ser Pro Lys Leu Lys Asn Gly Phe Pro His Pro Glu Pro Asp Cys Asn Pro Ser Glu Ala Ala Ser Glu Glu Ser Asn Ser Glu Ile Glu Gln Glu Ile Pro Val Glu Gln Lys Glu Gly Ala Phe Ser Asn Phe Pro Ile Ser Glu Glu 115 120 125 Thr Ile Lys Leu Leu Lys Gly Arg Gly Val Thr Phe Leu Phe Pro Ile 130 135 140 Gln Ala Lys Thr Phe His His Val Tyr Ser Gly Lys Asp Leu Ile Ala 145 150 155 160 Gln Ala Arg Thr Gly Thr Gly Lys Thr Phe Ser Phe Ala Ile Pro Leu 165 170 175 Ile Glu Lys Leu His Gly Glu Leu Gln Asp Arg Lys Arg Gly Arg Ala 180 185 190 Pro Gln Val Leu Val Leu Ala Pro Thr Arg Glu Leu Ala Asn Gln Val 195 200 205 Ser Lys Asp Phe Ser Asp Ile Thr Lys Lys Leu Ser Val Ala Cys Phe Tyr Gly Gly Thr Pro Tyr Gly Gly Gln Phe Glu Arg Met Arg Asn Gly 225 230 235 240 Ile Asp Ile Leu Val Gly Thr Pro Gly Arg Ile Lys Asp His Ile Glm Asn Gly Lys Leu Asp Leu Thr Lys Leu Lys His Val Val Leu Asp Glu 260 265 Val Asp Gln Met Leu Asp Met Gly Phe Ala Asp Gln Val Glu Glu Ile Leu Ser Val Ala Tyr Lys Lys Asp Ser Glu Asp Asn Pro Gln Thr Leu 290 295 300 Leu Phe Ser Ala Thr Cys Pro His Trp Val Phe Asn Val Ala Lys Lys 305 310 315 320 Tyr Met Lys Ser Thr Tyr Glu Gln Val Asp Leu Ile Gly Lys Lys Thr 325 330 335 Gln Lys Thr Ala Ile Thr Val Glu His Leu Ala Ile Lys Cys His Trp Thr Gln Arg Ala Ala Val Ile Gly Asp Val Ile Arg Val Tyr Ser Gly His Gln Gly Arg Thr Ile Ile Phe Cys Glu Thr Lys Lys Glu Ala Gln

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Leu Ser Gln Asn Ser Ala Ile Lys Gln Asp Ala Gln Ser Leu His
385 390 395 400

Gly Asp Ile Pro Gln Lys Gln Arg Glu Ile Thr Leu Lys Gly Phe Arg 405 410 415 Asn Gly Ser Phe Gly Val Leu Val Ala Thr Asn Val Ala Ala Arg Gly
420 425 430 Leu Asp Ile Pro Glu Val Asp Leu Val Ile Gln Ser Ser Pro Pro Lys 435 440 445 Asp Val Glu Ser Tyr Ile His Arg Ser Gly Arg Thr Gly Arg Ala Gly 450 455 460 Arg Thr Gly Val Cys Ile Cys Phe Tyr Gln His Lys Glu Glu Tyr Gln 465 470 475 480 Leu Val Gln Val Glu Gln Lys Ala Gly Ile Lys Phe Lys Arg Ile Gly 495 Val Pro Ser Ala Thr Glu Ile Ile Lys Ala Ser Ser Lys Asp Ala Ile Arg Leu Leu Asp Ser Val Pro Pro Thr Ala Ile Ser His Phe Lys Gln 515 520 525 Ser Ala Glu Lys Leu Ile Glu Glu Lys Gly Ala Val Glu Ala Leu Ala 530 540 Ala Ala Leu Ala His Ile Ser Gly Ala Thr Ser Val Asp Gln Arg Ser Leu Ile Asn Ser Asn Val Gly Phe Val Thr Met Ile Leu Gln Cys Ser 565 570 575 Ile Glu Met Pro Asn Ile Ser Tyr Ala Trp Lys Glu Leu Lys Glu Gln 580 585 590 Leu Gly Glu Glu Ile Asp Ser Lys Val Lys Gly Met Val Phe Leu Lys 595 600 605 Gly Lys Leu Gly Val Cys Phe Asp Val Pro Thr Ala Ser Val Thr Glu Ile Gln Glu Lys Trp His Asp Ser Arg Arg Trp Gln Leu Ser Val Ala 625 630 635 Thr Glu Gln Pro Glu Leu Glu Gly Pro Arg Glu Gly Tyr Gly Gly Phe
645 650 655 Arg Gly Gln Arg Glu Gly Ser Arg Gly Phe Arg Gly Gln Arg Asp Gly Asn Arg Arg Phe Arg Gly Gln Arg Glu Gly Ser Arg Gly Pro Arg Gly 675 685 Gln Arg Ser Gly Gly Gly Asn Lys Ser Asn Arg Ser Gln Asn Lys Gly Gln Lys Arg Ser Phe Ser Lys Ala Phe Gly Gln 710 715

<210> 120 <211> 294



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt PRT Homo sapiens <400> 120 Met Glu Asp Ser Met Asp Met Asp Met Ser Pro Leu Arg Pro Gln Asn 1 10 15 Tyr Leu Phe Gly Cys Glu Leu Lys Ala Asp Lys Asp Tyr His Phe Lys 20 30Val Asp Asp Glu Asp Glu His Gln Leu Ser Leu Arg Thr Val Ser Leu Gly Ala Gly Ala Lys Asp Glu Leu His Ile Val Glu Ala Glu Ala 50 60 Met Asn Tyr Glu Gly Ser Pro Ile Lys Val Thr Leu Ala Thr Leu Lys Met Ser Val Gln Pro Thr Val Ser Leu Gly Gly Phe Glu Ile Thr Pro Pro Val Val Leu Arg Leu Lys Cys Gly Ser Gly Pro Val His Ile Ser 100 105 110 Gly Gln His Leu Val Ala Val Glu Glu Asp Ala Glu Ser Glu Asp Glu 115 120 125 Glu Glu Glu Asp Val Lys Leu Leu Ser Ile Ser Gly Lys Arg Ser Ala 130 135 140 Pro Gly Gly Gly Ser Lys Val Pro Gln Lys Lys Val Lys Leu Ala Ala 145 150 160 Asp Glu Asp Asp Asp Asp Asp Glu Glu Asp Asp Glu Asp Asp Glu Asp Asp 175 Asp Asp Asp Phe Asp Asp Glu Glu Ala Glu Glu Lys Ala Pro Val Lys Lys Ser Ile Arg Asp Thr Pro Ala Lys Asn Ala Gln Lys Ser Asn 195 200 205Gln Asn Gly Lys Asp Ser Lys Pro Ser Ser Thr Pro Arg Ser Lys Gly 210 215 220 Gln Glu Ser Phe Lys Lys Gln Glu Lys Thr Pro Lys Thr Pro Lys Gly 225 230 240 Pro Ser Ser Val Glu Asp Ile Lys Ala Lys Met Gln Ala Ser Ile Glu Lys Gly Gly Ser Leu Pro Lys Val Glu Alá Lys Phe Ile Asn Tyr Val 260 265 270

<210> 121

<212> PRT <213> Homo sapiens

Gln Trp Arg Lys Ser Leu 290

Lys Asn Cys Phe Arg Met Thr Asp Gln Glu Ala Ile Gln Asp Leu Trp

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <400> 121 Met Ala Ala Gly Thr Ala Ala Ala Leu Ala Phe Leu Ser Gln Glu Ser 10 15 Arg Thr Arg Ala Gly Gly Val Gly Leu Arg Val Pro Ala Pro Val Thr Met Asp Ser Phe Phe Phe Gly Cys Glu Leu Ser Gly His Thr Arg 35 40 45Ser Phe Thr Phe Lys Val Glu Glu Glu Asp Asp Ala Glu His Val Leu 50 60 Ala Leu Thr Met Leu Cys Leu Thr Glu Gly Ala Lys Asp Glu Cys Asn 65 70 75 80 Val Val Glu Val Val Ala Arg Asn His Asp His Gln Glu Ile Ala Val Pro Val Ala Asn Leu Lys Leu Ser Cys Gln Pro Met Leu Ser Leu Asp 100 105 110 Asp Phe Gln Leu Gln Pro Pro Val Thr Phe Arg Leu Lys Ser Gly Ser 115 120 125 Gly Pro Val Arg Ile Thr Gly Arg His Gln Ile Val Thr Met Ser Asn 130 135 140 Asp Val Ser Glu Glu Glu Ser Glu Glu Glu Glu Asp Ser Asp Glu 145 150 155 160 Glu Glu Val Glu Leu Cys Pro Ile Leu Pro Ala Lys Lys Gln Gly Gly
165 170 175

Arg Pro

122 802 PRT

Homo sapiens

<400> 122

Met Pro Arg Ile Met Ile Lys Gly Gly Val Trp Arg Asn Thr Glu Asp 10 15Glu Ile Leu Lys Ala Ala Val Met Lys Tyr Gly Lys Asn Gln Trp Ser 25 30 Arg Ile Ala Ser Leu Leu His Arg Lys Ser Ala Lys Gln Cys Lys Ala 35 40 45 Arg Trp Tyr Glu Trp Leu Asp Pro Ser Ile Lys Lys Thr Glu Trp Ser 50 60Arg Glu Glu Glu Lys Leu Leu His Leu Ala Lys Leu Met Pro Thr 65 70 75 80 Gln Trp Arg Thr Ile Ala Pro Ile Ile Gly Arg Thr Ala Ala Gln Cys Leu Glu His Tyr Glu Phe Leu Leu Asp Lys Ala Ala Gln Arg Asp Asn Glu Glu Glu Thr Thr Asp Asp Pro Arg Lys Leu Lys Pro Gly Glu Ile

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 115 120 125 Asp Pro Asn Pro Glu Thr Lys Pro Ala Arg Pro Asp Pro Ile Asp Met 130 135 140 Asp Glu Asp Glu Leu Glu Met Leu Ser Glu Ala Arg Ala Arg Leu Ala 145 150 160 Asn Thr Gln Gly Lys Lys Ala Lys Arg Lys Ala Arg Glu Lys Gln Leu 165 170 175 Glu Glu Ala Arg Arg Leu Ala Ala Leu Gln Lys Arg Arg Glu Leu Arg 185 190 Ala Ala Gly Ile Glu Ile Gln Lys Lys Arg Lys Arg Lys Arg Gly Val 195 200 205 Asp Tyr Asn Ala Glu Ile Pro Phe Glu Lys Lys Pro Ala Leu Gly Phe 210 225 Tyr Asp Thr Ser Glu Glu Asn Tyr Gln Ala Leu Asp Ala Asp Phe Arg 225 230 235 240 Lys Leu Arg Gln Gln Asp Leu Asp Gly Glu Leu Arg Ser Glu Lys Glu 245 250 255 Gly Arg Asp Arg Lys Lys Asp Lys Gln His Leu Lys Arg Lys Lys Glu 265 270 Ser Asp Leu Pro Ser Ala Ile Leu Gln Thr Ser Gly Val Ser Glu Phe 275 280 285 Thr Lys Lys Arg Ser Lys Leu Val Leu Pro Ala Pro Gln Ile Ser Asp 290 300 Ala Glu Leu Gln Glu Val Val Lys Val Gly Gln Ala Ser Glu Ile Ala 305 310 315 320 Arg Gln Thr Ala Glu Glu Ser Gly Ile Thr Asn Ser Ala Ser Ser Thr Leu Leu Ser Glu Tyr Asn Val Thr Asn Asn Ser Val Ala Leu Arg Thr 340 345 350 Pro Arg Thr Pro Ala Ser Gln Asp Arg Ile Leu Gln Glu Ala Gln Asn 355 360 365 Leu Met Ala Leu Thr Asn Val Asp Thr Pro Leu Lys Gly Gly Leu Asn 370 380 Thr Pro Leu His Glu Ser Asp Phe Ser Gly Val Thr Pro Gln Arg Gln 385 390 395 400 Val Val Gln Thr Pro Asn Thr Val Leu Ser Thr Pro Phe Arg Thr Pro Ser Asn Gly Ala Glu Gly Leu Thr Pro Arg Ser Gly Thr Thr Pro Lys 420 425 430 Pro Val Ile Asn Ser Thr Pro Gly Arg Thr Pro Leu Arg Asp Lys Leu
435 440 445 Asn Ile Asn Pro Glu Asp Gly Met Ala Asp Tyr Ser Asp Pro Ser Tyr

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Val Lys Gln Met Glu Arg Glu Ser Arg Glu His Leu Arg Leu Gly Leu
465 470 480 Leu Gly Leu Pro Ala Pro Lys Asn Asp Phe Glu Ile Val Leu Pro Glu 485 490 495 Asn Ala Glu Lys Glu Leu Glu Glu Arg Glu Ile Asp Asp Thr Tyr Ile 500 505 510 Glu Asp Ala Ala Asp Val Asp Ala Arg Lys Gln Ala Ile Arg Asp Ala 515 520 525 Glu Arg Val Lys Glu Met Lys Arg Met His Lys Ala Val Gln Lys Asp 530 540 Leu Pro Arg Pro Ser Glu Val Asn Glu Thr Ile Leu Arg Pro Leu Asn 545 550 555 560 Val Glu Pro Pro Leu Thr Asp Leu Gln Lys Ser Glu Glu Leu Ile Lys
565 570 575 Lys Glu Met Ile Thr Met Leu His Tyr Asp Leu Leu His His Pro Tyr 580 585 590 Glu Pro Ser Gly Asn Lys Lys Gly Lys Thr Val Gly Phe Gly Thr Asn 595 600 605 Asn Ser Glu His Ile Thr Tyr Leu Glu His Asn Pro Tyr Glu Lys Phe Ser Lys Glu Glu Leu Lys Lys Ala Gln Asp Val Leu Val Gln Glu Met 625 630 635 640Glu Val Val Lys Gln Gly Met Ser His Gly Glu Leu Ser Ser Glu Ala 645 650 Tyr Asn Gln Val Trp Glu Glu Cys Tyr Ser Gln Val Leu Tyr Leu Pro Gly Gln Ser Arg Tyr Thr Arg Ala Asn Leu Ala Ser Lys Lys Asp Arg 675 680 685 Ile Glu Ser Leu Glu Lys Arg Leu Glu Ile Asn Arg Gly His Met Thr Thr Glu Ala Lys Arg Ala Ala Lys Met Glu Lys Lys Met Lys Ile Leu 705 710 715 720 Leu Gly Gly Tyr Gln Ser Arg Ala Met Gly Leu Met Lys Gln Leu Asn 730 735 Asp Leu Trp Asp Gln Ile Glu Gln Ala His Leu Glu Leu Arg Thr Phe Glu Glu Leu Lys Lys His Glu Asp Ser Ala Ile Pro Arg Leu Glu 755 760 765 Cys Leu Lys Glu Asp Val Gln Arg Gln Gln Glu Arg Glu Lys Glu Leu 770 780 Gln His Arg Tyr Ala Asp Leu Leu Leu Glu Lys Glu Thr Leu Lys Ser Lys Phe

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

<210> <211> <212> <213> Homo sapiens Met Gly Arg Lys Leu Asp Pro Thr Lys Glu Lys Arg Gly Pro Gly Arg Lys Ala Arg Lys Gln Lys Gly Ala Glu Thr Glu Leu Val Arg Phe Leu 20 25 30 Pro Ala Val Ser Asp Glu Asn Ser Lys Arg Leu Ser Ser Arg Ala Arg 35 40 45 Lys Arg Ala Ala Lys Arg Arg Leu Gly Ser Val Glu Ala Pro Lys Thr Asn Lys Ser Pro Glu Ala Lys Pro Ser Pro Gly Lys Leu Pro Lys Gly Ile Ser Ala Gly Ala Val Gln Thr Ala Gly Lys Lys Gly Pro Gln Ser Leu Phe Asn Ala Pro Arg Gly Lys Lys Arg Pro Ala Pro Gly Ser Asp $100 ext{ } 105 ext{ } 110$ Glu Glu Glu Glu Glu Asp Ser Glu Glu Asp Gly Met Val Asn His 115 120 125 Gly Asp Leu Trp Gly Ser Glu Asp Asp Ala Asp Thr Val Asp Asp Tyr 130 135 140 Gly Ala Asp Ser Asn Ser Glu Asp Glu Glu Glu Glu Glu Ala Leu Leu 145 150 155 160 Pro Ile Glu Arg Ala Ala Arg Lys Gln Lys Ala Arg Glu Ala Ala Ala 165 170 175 Gly Ile Gln Trp Ser Glu Glu Glu Thr Glu Asp Glu Glu Glu Glu Lys 180 185 190 Glu Val Thr Pro Glu Ser Gly Pro Pro Lys Val Glu Glu Ala Asp Gly 195 200 205 Gly Leu Gln Ile Asn Val Asp Glu Glu Pro Phe Val Leu Pro Pro Ala 210 225 220 Gly Glu Met Glu Gln Asp Ala Gln Ala Pro Asp Leu Gln Arg Val His 225 230 235 240 Lys Arg Ile Gln Asp Ile Val Gly Ile Leu Arg Asp Phe Gly Ala Gln $245 \hspace{0.5cm} 250 \hspace{0.5cm} 255$ Arg Glu Glu Gly Arg Ser Arg Ser Glu Tyr Leu Asn Arg Leu Lys Lys 260 265 270 Asp Leu Ala Ile Tyr Tyr Ser Tyr Gly Asp Phe Leu Leu Gly Lys Leu 275 280 285 Met Asp Leu Phe Pro Leu Ser Glu Leu Val Glu Phe Leu Glu Ala Asn

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Val Pro Arg Pro Val Thr Leu Arg Thr Asn Thr Leu Lys Thr Arg
305 310 315 320

Arg Arg Asp Leu Ala Gln Ala Leu Ile Asn Arg Gly Val Asn Leu Asp 325 330 335 Pro Leu Gly Lys Trp Ser Lys Thr Gly Leu Val Val Tyr Asp Ser Ser 340 345 Val Pro Ile Gly Ala Thr Pro Glu Tyr Leu Ala Gly His Tyr Met Leu 355 360 365 Gln Gly Ala Ser Ser Met Leu Pro Val Met Ala Leu Ala Pro Gln Glu His Glu Arg Ile Leu Asp Met Cys Cys Ala Pro Gly Gly Lys Thr Ser 385 390 395 400 Tyr Met Ala Gln Leu Met Lys Asn Thr Gly Val Ile Leu Ala Asn Asp 405 410 415 Ala Asn Ala Glu Arg Leu Lys Ser Val Val Gly Asn Leu His Arg Leu 425 430 Gly Val Thr Asn Thr Ile Ile Ser His Tyr Asp Gly Arg Gln Phe Pro
435 440 445 Lys Val Val Gly Gly Phe Asp Arg Val Leu Leu Asp Ala Pro Cys Ser Gly Thr Gly Val Ile Ser Lys Asp Pro Ala Val Lys Thr Asn Lys Asp 465 470 475 480 Glu Lys Asp Ile Leu Arg Cys Ala His Leu Gln Lys Glu Leu Leu Leu 485 490 495 Ser Ala Ile Asp Ser Val Asn Ala Thr Ser Lys Thr Gly Gly Tyr Leu
500 505 510 Val Tyr Cys Thr Cys Ser Ile Thr Val Glu Glu Asn Glu Trp Val Val 515 520 525 Asp Tyr Ala Leu Lys Lys Arg Asn Val Arg Leu Val Pro Thr Gly Leu 530 540 Asp Phe Gly Gln Glu Gly Phe Thr Arg Phe Arg Glu Arg Arg Phe His 545 550 560 Pro Ser Leu Arg Ser Thr Arg Arg Phe Tyr Pro His Thr His Asn Met 565 570 575 Asp Gly Phe Phe Ile Ala Lys Phe Lys Lys Phe Ser Asn Ser Ile Pro 580 585 Gln Ser Gln Thr Gly Asn Ser Glu Thr Ala Thr Pro Thr Asn Val Asp 595 600 605 Leu Pro Gln Val Ile Pro Lys Ser Glu Asn Ser Ser Gln Pro Ala Lys Lys Ala Lys Gly Ala Ala Lys Thr Lys Gln Gln Leu Gln Lys Gln Gln 635 640 His Pro Lys Lys Ala Ser Phe Gln Lys Leu Asn Gly Ile Ser Lys Gly 645 650 655



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Asp Ser Glu Leu Ser Thr Val Pro Ser Val Thr Lys Thr Gln Ala 660 665 670 Ser Ser Ser Phe Gln Asp Ser Ser Gln Pro Ala Gly Lys Ala Glu Gly 675 680 685 Ile Arg Glu Pro Lys Val Thr Gly Lys Leu Lys Gln Arg Ser Pro Lys 690 700 Leu Gln Ser Ser Lys Lys Val Ala Phe Leu Arg Gln Asn Ala Pro Pro 705 710 715 720 Lys Gly Thr Asp Thr Gln Thr Pro Ala Val Leu Ser Pro Ser Lys Thr 725 730 735 Gln Ala Thr Leu Lys Pro Lys Asp His His Gln Pro Leu Gly Arg Ala $740 \hspace{1.5cm} 750 \hspace{1.5cm}$ Lys Gly Val Glu Lys Gln Gln Phe Ala Glu Gln Pro Phe Glu Lys Ala 755 760 765 Ala Phe Gln Lys Gln Asn Asp Thr Pro Lys Gly Leu Ser Leu Pro Leu 770 780 Cys Leu Pro Ser Val Pro Ala Ala Pro His Gln Gln Arg Gly Arg Asn 785 790 795 Leu Ser Pro Gly Ala Thr Ala Ser Cys Cys Tyr Leu Arg Trp Leu Lys 805 810 815 Thr Arg Arg Val Ala His Cys His Cys His Gln Val Gly Thr Leu Ala Ser Val Arg Met Pro Ser Leu Leu Cys Ile Pro Met Lys Phe Asn Thr 835 840 845 His Phe Lys Thr Ser Gly His 850 855

<210> 124 <211> 1884 <212> PRT <213> Homo sapiens

val Ala Gly Cys Arg Arg Arg Gly Ala Gly Asp Pro Asn Met Ala Asn 10 15 Glu Lys Ala Phe Gln Gln Ser Val Glu Gln Asp Asn Leu Phe Asp Ile 35 40 45 Ser Thr Glu Glu Gly Ser Thr Lys Arg Lys Lys Ser Gln Lys Gly Pro 50 60Ala Lys Thr Lys Lys Leu Lys Ile Glu Lys Arg Glu Ser Ser Lys Ser Ala Arg Glu Lys Phe Glu Ile Leu Ser val Glu Ser Leu Cys Glu Gly 85 90 95 Met Arg Ile Leu Gly Cys Val Lys Glu Val Asn Glu Leu Glu Leu Val

Protein Complexes of cellular networks underlying the development of cancer and other diseases. ST25.txt 100 105 110Ile Ser Leu Pro Asn Gly Leu Gln Gly Phe Val Gln Val Thr Glu Ile 115 120 125 Cys Asp Ala Tyr Thr Lys Lys Leu Asn Glu Gln Val Thr Gln Glu Gln Pro Leu Lys Asp Leu Leu His Leu Pro Glu Leu Phe Ser Pro Gly Met 145 150 155 160 Leu Val Arg Cys Val Val Ser Ser Leu Gly Ile Thr Asp Arg Gly Lys 165 170 175 Lys Ser Val Lys Leu Ser Leu Asn Pro Lys Asn Val Asn Arg Val Leu 180 185 Ser Ala Glu Ala Leu Lys Pro Gly Met Leu Leu Thr Gly Thr Val Ser 195 200 205 Ser Leu Glu Asp His Gly Tyr Leu Val Asp Ile Gly Val Asp Gly Thr Arg Ala Phe Leu Pro Leu Leu Lys Ala Gln Glu Tyr Ile Arg Gln Lys 225 230 235 240 Asn Lys Gly Ala Lys Leu Lys Val Gly Gln Tyr Leu Asn Cys Ile Val 245 250 255 Glu Lys Val Lys Gly Asn Gly Gly Val Val Ser Leu Ser Val Gly His 260 265 270 Ser Glu Val Ser Thr Ala Ile Ala Thr Glu Gln Gln Ser Trp Asn Leu 275 280 285 Asn Asn Leu Leu Pro Gly Leu Val Val Lys Ala Gln Val Gln Lys Val 290 295 300 Thr Pro Phe Gly Leu Thr Leu Asn Phe Leu Thr Phe Phe Thr Gly Val 305 310 320 Val Asp Phe Met His Leu Asp Pro Lys Lys Ala Gly Thr Tyr Phe Ser Asn Gln Ala Val Arg Ala Cys Ile Leu Cys Val His Pro Arg Thr Arg $340 \ \ 345 \ \ \ 350$ Val Val His Leu Ser Leu Arg Pro Ile Phe Leu Gln Pro Gly Arg Pro 355 360 365 Leu Thr Arg Leu Ser Cys Gln Asn Leu Gly Ala Val Leu Asp Asp Val Pro val Gln Gly Phe Phe Lys Lys Ala Gly Ala Thr Phe Arg Leu Lys 385 390 395 400 Asp Gly Val Leu Ala Tyr Ala Arg Leu Ser His Leu Ser Asp Ser Lys 405 410 415Asn val Phe Asn Pro Glu Ala Phe Lys Pro Gly Asn Thr His Lys Cys Arg Ile Asp Tyr Ser Gln Met Asp Glu Leu Ala Leu Leu Ser Leu 435 440 445

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Arg Thr Ser Ile Ile Glu Ala Gln Tyr Leu Arg Tyr His Asp Ile Glu
450
450
460

Pro Gly Ala Val Val Lys Gly Thr Val Leu Thr Ile Lys Ser Tyr Gly 465 470 475 Met Leu Val Lys Val Gly Glu Gln Met Arg Gly Leu Val Pro Pro Met 490 495 His Leu Ala Asp Ile Leu Met Lys Asn Pro Glu Lys Lys Tyr His Ile 500 505 510 Gly Asp Glu Val Lys Cys Arg Val Leu Leu Cys Asp Pro Glu Ala Lys . 515 520 525 Lys Leu Met Met Thr Leu Lys Lys Thr Leu Ile Glu Ser Lys Leu Pro val Ile Thr Cys Tyr Ala Asp Ala Lys Pro Gly Leu Gln Thr His Gly 545 550 560Phe Ile Ile Arg Val Lys Asp Tyr Gly Cys Ile Val Lys Phe Tyr Asn 565 570 575 Asn Val Gln Gly Leu Val Pro Lys His Glu Leu Ser Thr Glu Tyr Ile 580 585 590 Pro Asp Pro Glu Arg Val Phe Tyr Thr Gly Gln Val Val Lys Val Val 595 600 605 Val Leu Asn Cys Glu Pro Ser Lys Glu Arg Met Leu Leu Ser Phe Lys 610 615 620 Leu Ser Ser Asp Pro Glu Pro Lys Lys Glu Pro Ala Gly His Ser Gln 625 630 635 Lys Lys Gly Lys Ala Ile Asn Ile Gly Gln Leu Val Asp Val Lys Val 645 655 Leu Glu Lys Thr Lys Asp Gly Leu Glu Val Ala Val Leu Pro His Asn $660 \hspace{1.5cm} 665 \hspace{1.5cm} 670$ Ile Arg Ala Phe Leu Pro Thr Ser His Leu Ser Asp His Val Ala Asn 675 680 685 Gly Pro Leu Leu His His Trp Leu Gln Ala Gly Asp Ile Leu His Arg 690 695 700 Val Leu Cys Leu Ser Gln Ser Glu Gly Arg Val Leu Leu Cys Arg Lys 715 720 Pro Ala Leu Val Ser Thr Val Glu Gly Gly Gln Asp Pro Lys Asn Phe Ser Glu Ile His Pro Gly Met Leu Leu Ile Gly Phe Val Lys Ser Ile 740 745 Pho Val Lys Ser Ile Lys Asp Tyr Gly Val Phe Ile Gln Phe Pro Ser Gly Leu Ser Gly Leu 765 760 765 Ala Pro Lys Ala Ile Met Ser Asp Lys Phe Val Thr Ser Thr Ser Asp 770 780 His Phe Val Glu Gly Gln Thr Val Ala Ala Lys Val Thr Asn Val Asp

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 785 790 795 800 Glu Glu Lys Gln Arg Met Leu Leu Ser Leu Arg Leu Ser Asp Cys Gly 805 810 815 Leu Gly Asp Leu Ala Ile Thr Ser Leu Leu Leu Leu Asn Gln Cys Leu 820 825 830 Glu Glu Leu Gln Gly Val Arg Ser Leu Met Ser Asn Arg Asp Ser Val 835 840 845 Leu Ile Gln Thr Leu Ala Glu Met Thr Pro Gly Met Phe Leu Asp Leu $850 \ \ 855 \ \ \ 860$ Val Val Glu Val Leu Glu Asp Gly Ser Val Val Phe Ser Gly Gly 865 870 875 Pro Val Pro Asp Leu Val Leu Lys Ala Ser Arg Tyr His Arg Ala Gly 885 890 895 Gln Glu Val Glu Ser Gly Gln Lys Lys Lys Val Val Ile Leu Asn Val Asp Leu Leu Lys Leu Glu Val His Val Ser Leu His Gln Asp Leu Val 915 920 925 Asn Arg Lys Ala Arg Lys Leu Arg Lys Gly Ser Glu His Gln Ala Ile $930 \hspace{1.5cm} 940$ Val Gln His Leu Glu Lys Ser Phe Ala Ile Ala Ser Leu Val Glu Thr Gly His Leu Ala Ala Phe Ser Leu Thr Ser His Leu Asn Asp Thr Phe Arg Phe Asp Ser Glu Lys Leu Gln Val Gly Gln Gly Val Ser Leu Thr 980 985 Leu Lys Thr Thr Glu Pro Gly Val Thr Gly Leu Leu Leu Ala Val Glu 995 1000 1005 Gly Pro Ala Ala Lys Arg Thr Met Arg Pro Thr Gln Lys Asp Ser 1010 1020 Glu Thr Val Asp Glu Asp Glu Glu Val Asp Pro Ala Leu Thr Val 1075 1030 1035 Gly Thr Ile Lys Lys His Thr Leu Ser Ile Gly Asp Met Val Thr 1040 1050 Gly Thr Val Lys Ser Ile Lys Pro Thr His Val Val Thr Leu 1055 1060 1065 Glu Asp Gly Ile Ile Gly Cys Ile His Ala Ser His Ile Leu Asp 1070 1080 Asp val Pro Glu Gly Thr Ser Pro Thr Thr Lys Leu Lys Val Gly Lys Thr Val Thr Ala Arg Val $\mbox{ Ile Gly Gly Arg Asp Met Lys Thr} 1100 11105$ Phe Lys Tyr Leu Pro Ile Ser His Pro Arg Phe Val Arg Thr Ile

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Pro Glu Leu Ser Val Arg Pro Ser Glu Leu Glu Asp Gly His Thr
1130 1135 1140

Ala Leu Asn Thr His Ser Val Ser Pro Met Glu Lys Ile Lys Gln 1145 1150 Tyr Gln Ala Gly Gln Thr Val Thr Cys Phe Leu Lys Lys Tyr Asn 1160 1165 1170 Val Val Lys Lys Trp Leu Glu Val Glu Ile Ala Pro Asp Ile Arg 1175 1180 1185 Gly Arg Ile Pro Leu Leu Leu Thr Ser Leu Ser Phe Lys Val Leu 1190 1200 Lys His Pro Asp Lys Lys Phe Arg Val Gly Gln Ala Leu Arg Ala 1205 1210 1215 Thr Val Val Gly Pro Asp Ser Ser Lys Thr Phe Leu Cys Leu Ser 1220 1230 Leu Thr Gly Pro His Lys Leu Glu Glu Glu Glu Val Ala Met Gly 1235 1240 1245 Arg Val Val Lys Val Thr Pro Asn Glu Gly Leu Thr Val Ser Phe Pro Phe Gly Lys Ile Gly Thr Val Ser Ile Phe His Met Ser Asp 1265 1270 1275 Ser Tyr Ser Glu Thr Pro Leu Glu Asp Phe Val Pro Gln Lys Val 1280 1290 Val Arg Cys Tyr Ile Leu Ser Thr Ala Asp Asn Val Leu Thr Leu Ser Leu Arg Ser Ser Arg Thr Asn Pro Glu Thr Lys Ser Lys Val Glu Asp Pro Glu Ile Asn Ser Ile Gln Asp Ile Lys Glu Gly Gln 1325 1330 1335 Leu Leu Arg Gly Tyr Val Gly Ser Ile Gln Pro His Gly Val Phe 1340 1350 Phe Arg Leu Gly Pro Ser Val Val Gly Leu Ala Arg Tyr Ser His 1355 1360 1365 Val Ser Gln His Ser Pro Ser Lys Lys Ala Leu Tyr Asn Lys His Leu Pro Glu Gly Lys Leu Leu Thr Ala Arg Val Leu Arg Leu Asn 1385 1390 1395 His Gln Lys Asn Leu Val Glu Leu Ser Phe Leu Pro Gly Asp Thr 1400 1405 1410

Gly Lys Pro Asp Val Leu Ser Ala Ser Leu Glu Gly Gln Leu Thr

Lys Gln Glu Glu Arg Lys Thr Glu Ala Glu Glu Arg Asp Gln Lys

Gly Glu Lys Lys Asn Gln Lys Arg Asn Glu Lys Lys Asn Gln Lys

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 1445 1450 1455

Gly Gln Glu Glu Val Glu Met Pro Ser Lys Glu Lys Gln Gln Pro 1460 1465 1470

Gln Lys Pro Gln Ala Gln Lys Arg Gly Gly Arg Glu Cys Arg Glu 1475 1480 1485

Ser Gly Ser Glu Gln Glu Arg Val Ser Lys Lys Pro Lys Lys Ala 1490 1500

Gly Leu Ser Glu Glu Asp Asp Ser Leu Val Asp Val Tyr Tyr Arg 1505 1510 1515

Glu Gly Lys Glu Glu Ala Glu Glu Thr Asn Val Leu Pro Lys Glu

Lys Gln Thr Lys Pro Ala Glu Ala Pro Arg Leu Gln Leu Ser Ser 1535 1540 1545

Gly Phe Ala Trp Asn Val Gly Leu Asp Ser Leu Thr Pro Ala Leu

Pro Pro Leu Ala Glu Ser Ser Asp Ser Glu Glu Asp Glu Lys Pro 1575 1570 1575

His Gln Ala Thr Ile Lys Lys Ser Lys Lys Glu Arg Glu Leu Glu 1580 1590

Lys Gln Lys Ala Glu Lys Glu Leu Ser Arg Ile Glu Glu Ala Leu 1595 1600 1605

Met Asp Pro Gly Arg Gln Pro Glu Ser Ala Asp Asp Phe Asp Arg

Leu Val Leu Ser Ser Pro Asn Ser Ser Ile Leu Trp Leu Gln Tyr 1625 1630 1635

Met Ala Phe His Leu Gln Ala Thr Glu Ile Glu Lys Ala Arg Ala 1640 1650

Val Ala Glu Arg Ala Leu Lys Thr Ile Ser Phe Arg Glu Glu Gln 1655 1660 1665

Glu Lys Leu Asn Val Trp Val Ala Leu Leu Asn Leu Glu Asn Met 1670 1680

Tyr Gly Ser Gln Glu Ser Leu Thr Lys Val Phe Glu Arg Ala Val 1685 1690 1695

Gln Tyr Asn Glu Pro Leu Lys Val Phe Leu His Leu Ala Asp Ile 1700 1705

Tyr Ala Lys Ser Glu Lys Phe Gln Glu Ala Gly Glu Leu Tyr Asn 1715 1720 1725

Arg Met Leu Lys Arg Phe Arg Gln Glu Lys Ala Val Trp Ile Lys 1730 1740

Tyr Gly Ala Phe Leu Leu Arg Arg Ser Gln Ala Ala Ser His 1745 1750 1755

Arg Val Leu Gln Arg Ala Leu Glu Cys Leu Pro Ser Lys Glu His 1760 1770

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Val Asp Val Ile Ala Lys Phe Ala Gln Leu Glu Phe Gln Leu Gly

1775 1780 1785

Asp Ala Glu Arg Ala Lys Ala Ile Phe Glu Asn Thr Leu Ser Thr 1790 1795 1800

Tyr Pro Lys Arg Thr Asp Val Trp Ser Val Tyr Ile Asp Met Thr 1805 1810 1815

Ile Lys His Gly Ser Gln Lys Asp Val Arg Asp Ile Phe Glu Arg 1820 1830

Val Ile His Leu Ser Leu Ala Pro Lys Arg Met Lys Phe Phe 1835 1840 1845

Lys Arg Tyr Leu Asp Tyr Glu Lys Gln His Gly Thr Glu Lys Asp 1850 1860

Val Gln Ala Val Lys Ala Lys Ala Leu Glu Tyr Val Glu Ala Lys 1865 1870 1875

Ser Ser Val Leu Glu Asp 1880

<400> 125

Lys Arg Lys Arg Glu Trp Ser Asp Glu Ser Glu Glu Glu Pro Glu Lys 1 10 15

Glu Leu Ala Pro Glu Pro Glu Glu Thr Trp Val Val Glu Thr Leu Cys 20 25 30

Gly Leu Lys Met Lys Leu Lys Gln Gln Arg Val Ser Pro Ile Leu Leu $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Glu His His Lys Asp Phe Asn Ser Gln Leu Ala Pro Gly Val Asp Pro 50 55

Ser Pro Pro His Arg Ser Phe Cys Trp Lys Arg Lys Met Glu Trp Trp 65 75 80

Asp Lys Ser Glu Glu Ser Glu Glu Glu Pro Arg Lys Val Leu Ala Pro 85 90 95

Glu Pro Glu Glu Ile Trp Val Ala Glu Met Leu Cys Gly Leu Lys Met 100 105 110

Lys Leu Lys Arg Arg Arg Val Ser Leu Val Leu Pro Glu His His Glu 115 120 125

Ala Phe Asn Arg Leu Leu Glu Asp Pro Val Ile Lys Arg Phe Leu Ala 130 135 140

Trp Asp Lys Asp Leu Arg Val Ser Asp Lys Tyr Leu Leu Ala Met Val

Ile Ala Tyr Phe Ser Arg Ala Gly Phe Pro Ser Trp Gln Tyr Gln Arg 165 170 175

Leu His Phe Phe Leu Ala Leu Tyr Leu Ala Asn Asp Met Glu Glu Asp 180 185 190

<210> 125

<211> 30

<212> PRT
<213> Homo sapiens

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asp Glu Asp Ser Lys Gln Asn Ile Phe His Phe Leu Tyr Gly Lys Asn 205

Arg Ser Arg Ile Pro Leu Leu Arg Lys Arg Arg Phe Gln Leu Tyr Arg 210

Ser Met Asn Pro Arg Ala Arg Lys Asn Arg Ser His Ile Pro Leu Val 240

Arg Lys Arg Arg Phe Gln Leu Arg Arg Cys Met Asn Pro Arg Ala Arg 255

Lys Asn Arg Ser Gln Ile Val Leu Phe Gln Lys Arg Arg Phe His Phe 260

Phe Cys Ser Met Ser Cys Arg Ala Trp Val Ser Pro Glu Glu Leu Glu 285

Glu Ile Gln Ala Tyr Asp Pro Glu His Trp Val Trp Ala Arg Asp Arg Ala Arg Leu Ser 305

<210> 126 <211> 198

<212> PKI <213> Homo sapiens

<400> 126

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
180 185 190

Asp Arg Tyr Glu Glu Ile 195

127 276 PRT

Homo sapiens

<400>

Met Gln Asp Leu Arg Met Leu Met Pro His Ser Lys Ala Asp Thr Lys 1 10

Met Asp Arg Lys Asp Lys Leu Phe Val Ile Asn Glu Val Cys Glu Met

Lys Asn Cys Asn Lys Cys Ile Tyr Phe Glu Ala Lys Lys Lys Gln Asp

Leu Tyr Met Trp Leu Ser Asn Ser Pro His Gly Pro Ser Ala Lys Phe $50 \hspace{1.5cm} 60$

Leu Val Gln Asn Ile His Thr Leu Ala Glu Leu Lys Met Thr Gly Asn 65 70 75 80

Cys Leu Lys Gly Ser Arg Pro Leu Leu Ser Phe Asp Pro Ala Phe Asp 90 95

Glu Leu Pro His Tyr Ala Leu Leu Lys Glu Leu Leu Ile Gln Ile Phe 100 105 110

Ser Thr Pro Arg Tyr His Pro Lys Ser Gln Pro Phe Val Asp His Val 115 120 125

Phe Thr Phe Thr Ile Leu Asp Asn Arg Ile Trp Phe Arg Asn Phe Gln

Ile Ile Glu Glu Asp Ala Ala Leu Val Glu Ile Gly Pro Arg Phe Val 145 150 155 160

Leu Asn Leu Ile Lys Ile Phe Gln Gly Ser Phe Gly Gly Pro Thr Leu 165 170 175

Tyr Glu Asn Pro His Tyr Gln Ser Pro Asn Met His Arg Arg Val Ile 180 185 190

Arg Ser Ile Thr Ala Ala Lys Tyr Arg Glu Lys Gln Gln Val Lys Asp 195 200 205

Val Gln Lys Leu Arg Lys Lys Glu Pro Lys Thr Leu Leu Pro His Asp 210 215 220

Pro Thr Ala Asp Val Phe Val Thr Pro Ala Glu Glu Lys Pro Ile Glu 225 230 235 240

Ile Gln Trp Val Lys Pro Glu Pro Lys Val Asp Leu Lys Ala Arg Lys 245 250 255

Lys Arg Ile Tyr Lys Arg Gln Arg Lys Met Lys Gln Arg Met Asp Ser

Gly Lys Thr Lys

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <210> 128 <211> 297 <212> PRT <213> Homo sapiens <400> 128 Met Glu Asp Tyr Thr Lys Ile Glu Lys Ile Gly Glu Gly Thr Tyr Gly
10 15 Val Val Tyr Lys Gly Arg His Lys Thr Thr Gly Gln Val Val Ala Met 20 25 30 Lys Lys Ile Arg Leu Glu Ser Glu Glu Glu Gly Val Pro Ser Thr Ala 35 40 45 lle Arg Glu Ile Ser Leu Leu Lys Glu Leu Arg His Pro Asn Ile Val Ser Leu Gln Asp Val Leu Met Gln Asp Ser Arg Leu Tyr Leu Ile Phe 65 70 75 80 Glu Phe Leu Ser Met Asp Leu Lys Lys Tyr Leu Asp Ser Ile Pro Pro Gly Gln Tyr Met Asp Ser Ser Leu Val Lys Ser Tyr Leu Tyr Gln Ile $100 \hspace{1cm} 105 \hspace{1cm} 110$ Leu Gln Gly Ile Val Phe Cys His Ser Arg Arg Val Leu His Arg Asp 115 125 125Leu Lys Pro Gln Asn Leu Leu Ile Asp Asp Lys Gly Thr Ile Lys Leu 130 140 Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Ile Pro Ile Arg Val Tyr 145 150 160 Thr His Glu Val Val Thr Leu Trp Tyr Arg Ser Pro Glu Val Leu Leu 165 170 175 Gly Ser Ala Arg Tyr Ser Thr Pro Val Asp Ile Trp Ser Ile Gly Thr $180 \hspace{1cm} 185 \hspace{1cm} 190$ Ile Phe Ala Glu Leu Ala Thr Lys Lys Pro Leu Phe His Gly Asp Ser

Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Ala Leu Gly Thr Pro Asn 210 225 220

Asn Glu Val Trp Pro Glu Val Glu Ser Leu Gln Asp Tyr Lys Asn Thr 225 230 235 240

Phe Pro Lys Trp Lys Pro Gly Ser Leu Ala Ser His Val Lys Asn Leu 245 250 255

Asp Glu Asn Gly Leu Asp Leu Leu Ser Lys Met Leu Ile Tyr Asp Pro

Ala Lys Arg Ile Ser Gly Lys Met Ala Leu Asn His Pro Tyr Phe Asn 275 280 285

Asp Leu Asp Asn Gln Ile Lys Lys Met 290 295

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <213> Homo sapiens

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<400>

Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly 10 15

Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu 20 25 30

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val 50 55 60

Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe

Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu $85 \hspace{1cm} 90 \hspace{1cm} 95$

Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu $100 \hspace{1cm} 105 \hspace{1cm} 110$

Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu 115 120 125

Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala

Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr 145 150 160

His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly 165 170 175

Cys Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile 180 185 190

Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu 195 200 205

Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu 210 215 220

Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe 225 230 235 240

Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp 245 250 250

Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn 260 265 770

Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp 275 280 285

Val Thr Lys Pro Val Pro His Leu Arg Leu 290 295

Homo sapiens

<400>

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Met Asp Ala Leu Cys Gly Ser Gly Glu Leu Gly Ser Lys Phe Trp Asp Ser Asn Leu Ser Val His Thr Glu Asn Pro Asp Leu Thr Pro Cys Phe Gln Asn Ser Leu Leu Ala Trp Val Pro Cys Ile Tyr Leu Trp Val Ala Ile Leu Ser His Leu Ser Lys Leu Lys Met Val Leu Gly Val Leu Leu 65 70 75 80 Trp Cys Val Ser Trp Ala Asp Leu Phe Tyr Ser Phe His Gly Leu Val His Gly Arg Ala Pro Ala Pro Val Phe Phe Val Thr Pro Leu Val Val 100 105 110 Gly Val Thr Met Leu Leu Ala Thr Leu Leu Ile Gln Tyr Glu Arg Leu 115 120 125 Gln Gly Val Gln Ser Ser Gly Val Leu Ile Ile Phe Trp Phe Leu Cys 130 140 Val Val Cys Ala Ile Val Pro Phe Arg Ser Lys Ile Leu Leu Ala Lys 145 150 160 Ala Glu Gly Glu Ile Ser Asp Pro Phe Arg Phe Thr Thr Phe Tyr Ile 165 170 175 His Phe Ala Leu Val Leu Ser Thr Leu Ile Leu Ala Cys Phe Arg Glu 180 185 190 Lys Pro Pro Phe Phe Ser Ala Lys Asn Val Asp Pro Asn Pro Tyr Pro 195 200 205 Glu Thr Ser Ala Gly Phe Leu Ser Arg Leu Phe Phe Trp Trp Phe Thr 210 220 Lys Met Ala Ile Tyr Gly Tyr Arg His Pro Leu Glu Glu Lys Asp Leu 225 230 235 240 Trp Ser Leu Lys Glu Glu Asp Arg Ser Gln Met Val Val Gln Gln Leu 245 250 255 Leu Glu Ala Trp Arg Lys Gln Glu Lys Gln Thr Ala Arg His Lys Ala 260 265 270 Ser Ala Ala Pro Gly Lys Asn Ala Ser Gly Glu Asp Glu Val Leu Leu 275 280 285 Gly Ala Arg Pro Arg Pro Arg Lys Pro Ser Phe Leu Lys Ala Leu Leu 290 295 300 Ala Thr Phe Gly Ser Ser Phe Leu Ile Ser Ala Cys Phe Lys Leu Ile 305 310 315 Gln Asp Leu Leu Ser Phe Ile Asn Pro Gln Leu Leu Ser Ile Leu Ile 325 330 335 Arg Phe Ile Ser Asn Pro Met Ala Pro Ser Trp Trp Gly Phe Leu Val

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 340 345 Ala Gly Leu Met Phe Leu Cys Ser Met Met Gln Ser Leu Ile Leu Gln 355 360 365 His Tyr Tyr His Tyr Ile Phe Val Thr Gly Val Lys Phe Arg Thr Gly 370 375 380 Ile Met Gly Val Ile Tyr Arg Lys Ala Leu Val Ile Thr Asn Ser Val 385 390 395 400 Lys Arg Ala Ser Thr Val Gly Glu Ile Val Asn Leu Met Ser Val Asp $405 \hspace{0.25cm} 410 \hspace{0.25cm} 410$ Ala Gln Arg Phe Met Asp Leu Ala Pro Phe Leu Asn Leu Leu Trp Ser 420 430 Ala Pro Leu Gln Ile Ile Leu Ala Ile Tyr Phe Leu Trp Gln Asn Leu 435 440 445 Gly Pro Ser Val Leu Ala Gly Val Ala Phe Met Val Leu Leu Ile Pro
450 460 Leu Asn Gly Ala Val Ala Val Lys Met Arg Ala Phe Gln Val Lys Gln 465 470 475 480 Met Lys Leu Lys Asp Ser Arg Ile Lys Leu Met Ser Glu Ile Leu Asn 485 490 495 Gly Ile Lys Val Leu Lys Leu Tyr Ala Trp Glu Pro Ser Phe Leu Lys 500 505 510 Gln Val Glu Gly Ile Arg Gln Gly Glu Leu Gln Leu Leu Arg Thr Ala 515 520 525 Ala Tyr Leu His Thr Thr Thr Thr Phe Thr Trp Met Cys Ser Pro Phe 530 540 Leu Val Thr Leu Ile Thr Leu Trp Val Tyr Val Tyr Val Asp Pro Asn 545 550 560 Asn Val Leu Asp Ala Glu Lys Ala Phe Val Ser Val Ser Leu Phe Asn 565 570 575 Ile Leu Arg Leu Pro Leu Asn Met Leu Pro Gln Leu Ile Ser Asn Leu 580 585 590 Thr Gln Ala Ser Val Ser Leu Lys Arg Ile Gln Gln Phe Leu Ser Gln 595 600 605 Glu Glu Leu Asp Pro Gln Ser Val Glu Arg Lys Thr Ile Ser Pro Gly 610 615 620Tyr Ala Ile Thr Ile His Ser Gly Thr Phe Thr Trp Ala Gln Asp Leu 625 630 635 Pro Pro Thr Leu His Ser Leu Asp Ile Gln Val Pro Lys Gly Ala Leu 645 650 Val Ala Val Val Gly Pro Val Gly Cys Gly Lys Ser Ser Leu Val Ser 660 665 670 Ala Leu Leu Gly Glu Met Glu Lys Leu Glu Gly Lys Val His Met Lys



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Gly Ser Val Ala Tyr Val Pro Gln Gln Ala Trp Ile Gln Asn Cys Thr

690

690

Leu Gln Glu Asn Val Leu Phe Gly Lys Ala Leu Asn Pro Lys Arg Tyr 705 710 715 720 Gln Gln Thr Leu Glu Ala Cys Ala Leu Leu Ala Asp Leu Glu Met Leu 725 730 735 Pro Gly Gly Asp Gln Thr Glu Ile Gly Glu Lys Gly Ile Asn Leu Ser 740 745 750 Gly Gly Gln Arg Gln Arg Val Ser Leu Ala Arg Ala Val Tyr Ser Asp 755 760 765 Ala Asp Ile Phe Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ser His 770 780 Val Ala Lys His Ile Phe Asp His Val Ile Gly Pro Glu Gly Val Leu 785 790 795 800 Ala Gly Lys Thr Arg Val Leu Val Thr His Gly Ile Ser Phe Leu Pro 805 810 815 Gln Thr Asp Phe Ile Ile Val Leu Ala Asp Gly Gln Val Ser Glu Met 820 825 830 Gly Pro Tyr Pro Ala Leu Leu Gln Arg Asn Gly Ser Phe Ala Asn Phe 835 840 845 Leu Cys Asn Tyr Ala Pro Asp Glu Asp Gln Gly His Leu Glu Asp Ser Trp Thr Ala Leu Glu Gly Ala Glu Asp Lys Glu Ala Leu Leu Ile Glu 865 870 875 Asp Thr Leu Ser Asn His Thr Asp Leu Thr Asp Asn Asp Pro Val Thr 895 Tyr Val Val Gln Lys Gln Phe Met Arg Gln Leu Ser Ala Leu Ser Ser 900 905 910 Asp Gly Glu Gly Gln Gly Arg Pro Val Pro Arg Arg His Leu Gly Pro 915 920 925 Ser Glu Lys Val Gln Val Thr Glu Ala Lys Ala Asp Gly Ala Leu Thr 930 940 Gln Glu Glu Lys Ala Ala Ile Gly Thr Val Glu Leu Ser Val Phe Trp 945 950 955 960 Asp Tyr Ala Lys Ala Val Gly Leu Cys Thr Thr Leu Ala Ile Cys Leu 965 970 975 Leu Tyr Val Gly Gln Ser Ala Ala Ala Ile Gly Ala Asn Val Trp Leu 980 985 990 Ser Ala Trp Thr Asn Asp Ala Met Ala Asp Ser Arg Gln Asn Asn Thr Ser Leu Arg Leu Gly Val Tyr Ala Ala Leu Gly Ile Leu Gln Gly Phe Leu Val Met Leu Ala Ala Met Ala Met Ala Ala Gly Gly Ile

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 1025 1030 1035

Gln Ala Ala Arg Val Leu His Gln Ala Leu Leu His Asn Lys Ile 1040 1045 1050

Arg Ser Pro Gln Ser Phe Phe Asp Thr Thr Pro Ser Gly Arg Ile 1055 1060 1065

Leu Asn Cys Phe Ser Lys Asp Ile Tyr Val Val Asp Glu Val Leu 1070 1080

Ala Pro Val Ile Leu Met Leu Leu Asn Ser Phe Phe Asn Ala Ile 1085 1090 1095

Ser Thr Leu Val Val Ile Met Ala Ser Thr Pro Leu Phe Thr Val

Val Ile Leu Pro Leu Ala Val Leu Tyr Thr Leu Val Gln Arg Phe 1115 1120 1125

Tyr Ala Ala Thr Ser Arg Gln Leu Lys Arg Leu Glu Ser Val Ser 1130 1140

Arg Ser Pro Ile Tyr Ser His Phe Ser Glu Thr Val Thr Gly Ala 1145 1150 1155

Ser Val $\mbox{ Ile Arg Ala Tyr Asn Arg Ser Arg Asp Phe} \mbox{ Glu Ile Ile} \mbox{ 1160} \mbox{ 1170}$

Ser Asp Thr Lys Val Asp Ala Asn Gln Arg Ser Cys Tyr Pro Tyr 1175 1180 1185

Ile Ile Ser Asn Arg Ser Glu Ala Ala Ser Leu Ala Pro Cys Ser 1190 1200

Ser Arg Asn Ser Gln Gln Ala Leu Trp Cys Ser Gly Ser Leu Ser 1205 1210 1215

Leu Leu Ser Pro Lys Gln Lys Thr Gly Pro Ala Leu Pro Leu Pro

His Phe Leu Leu Ile 1235

131 418 PRT Homo sapiens

Met Ala Gly Arg Leu Pro Ala Cys Val Val Asp Cys Gly Thr Gly Tyr 10 15

Thr Lys Leu Gly Tyr Ala Gly Asn Thr Glu Pro Gln Phe Ile Ile Pro 20 30

Ser Cys Ile Ala Ile Lys Glu Ser Ala Lys Val Gly Asp Gln Ala Gln

Arg Arg Val Met Lys Gly Val Asp Asp Leu Asp Phe Phe Ile Gly Asp

Glu Ala Ile Glu Lys Pro Thr Tyr Ala Thr Lys Trp Pro Ile Arg His

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gly Ile Val Glu Asp Trp Asp Leu Met Glu Arg Phe Met Glu Gln Val 85 90 95

Ile Phe Lys Tyr Leu Arg Ala Glu Pro Glu Asp His Tyr Phe Leu Leu 100 105 110 Thr Glu Pro Pro Leu Asn Thr Pro Glu Asn Arg Glu Tyr Thr Ala Glu 115 120 125Ile Met Phe Glu Ser Phe Asn Val Pro Gly Leu Tyr Ile Ala Val Gln
130 140 Ala Val Leu Ala Leu Ala Ala Ser Trp Thr Ser Arg Gln Val Gly Glu
145 150 160 Arg Thr Leu Thr Gly Thr Val Ile Asp Ser Gly Asp Gly Val Thr His 165 170 175 val Ile Pro Val Ala Glu Gly Tyr Val Ile Gly Ser Cys Ile Lys His 180 185 190 Ile Pro Ile Ala Gly Arg Asp Ile Thr Tyr Phe Ile Gln Gln Leu Leu Arg Asp Arg Glu Val Gly Ile Pro Pro Glu Gln Ser Leu Glu Thr Ala Lys Ala Val Lys Glu Arg Tyr Ser Tyr Val Cys Pro Asp Leu Val Lys 225 230 235 240 Glu Phe Asn Lys Tyr Asp Thr Asp Gly Ser Lys Trp Ile Lys Gln Tyr 245 250 255 Thr Gly Ile Asn Ala Ile Ser Lys Lys Glu Phe Ser Ile Asp Val Gly 265 270 Tyr Glu Arg Phe Leu Gly Pro Glu Ile Phe Phe His Pro Glu Phe Ala Asn Pro Asp Phe Thr Gln Pro Ile Ser Glu Val Val Asp Glu Val Ile Gln Asn Cys Pro Ile Asp Val Arg Arg Pro Leu Tyr Lys Asn Ile Val 305 310 315 320 Leu Ser Gly Gly Ser Thr Met Phe Arg Asp Phe Gly Arg Arg Leu Gln 335 Arg Asp Leu Lys Arg Thr Val Asp Ala Arg Leu Lys Leu Ser Glu Glu 340 345 Leu Ser Gly Gly Arg Leu Lys Pro Lys Pro Ile Asp Val Gln Val Ile $355 \hspace{1.5cm} 360 \hspace{1.5cm} 365$ Thr His His Met Gln Arg Tyr Ala Val Trp Phe Gly Gly Ser Met Leu Ala Ser Thr Pro Glu Phe Tyr Gln Val Cys His Thr Lys Lys Asp Tyr 385 390 395 400 Glu Glu Ile Gly Pro Ser Ile Cys Arg His Asn Pro Val Phe Gly Val

Met Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

132 210

Homo sapiens

<400> 132

Met Phe Glu Ser Phe Asn Val Pro Gly Leu Tyr Ile Ala Val Gln Ala 1 5 10 15

Val Leu Ala Leu Ala Ala Ser Trp Thr Ser Arg Gln Val Gly Glu Arg 20 25 30

Thr Leu Thr Gly Ile Val Ile Asp Ser Gly Asp Gly Val Thr His Val 35 40 45

Ile Pro Val Ala Glu Gly Tyr Val Ile Gly Ser Cys Ile Lys His Ile $50 \hspace{1cm} 60$

Pro Ile Ala Gly Arg Asp Ile Thr Tyr Phe Ile Gln Gln Leu Leu Arg 65 70 75 80

Glu Arg Glu Val Gly Ile Pro Pro Glu Gln Ser Leu Glu Thr Ala Lys $90 \hspace{1cm} 95$

Phe Ala Lys Tyr Asp Val Asp Pro Gln Lys Trp Ile Lys Gln Tyr Thr 115 120 125

Gly Ile Asn Ala Ile Asn Gln Lys Lys Phe Val Ile Asp Val Gly Tyr 130 135 140

Glu Arg Phe Leu Gly Pro Glu Ile Phe Phe His Pro Glu Phe Ala Asn 145 150 155 160

Pro Asp Ser Met Glu Ser Ile Ser Asp Val Val Asp Glu Val Ile Gln 165 170 175

Asn Cys Pro Ile Asp Val Arg Arg Pro Leu Tyr Lys Met Glu Gln Ile 180 185 190

Pro Leu Ser Tyr Pro Gln Gly His Gly Phe His Pro Leu Ser Pro Pro 195 200 205

Phe His

133 300 PRT

Homo sapiens

<400> 133

Met Ile Leu Leu Glu Val Asn Asn Arg Ile Ile Glu Glu Thr Leu Ala $1 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Leu Lys Phe Glu Asn Ala Ala Ala Gly Asn Lys Pro Glu Ala Val Glu 20 25 30

Val Thr Phe Ala Asp Phe Asp Gly Val Leu Tyr His Ile Ser Asn Pro $35 \qquad 40 \qquad 45$

Asn Gly Asp Lys Thr Lys Val Met Val Ser Ile Ser Leu Lys Phe Tyr

Protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Lys Glu Leu Gln Ala His Gly Ala Asp Glu Leu Leu Lys Arg Val Tyr Gly Ser Phe Leu Val Asn Pro Glu Ser Gly Tyr Asn Val Ser Leu Leu 85 90 95 Tyr Asp Leu Glu Asn Leu Pro Ala Ser Lys Asp Ser Ile Val His Gln
100 105 110 Ala Gly Met Leu Lys Arg Asn Cys Phe Ala Ser Val Phe Glu Lys Tyr 115 125 125Phe Gln Phe Gln Glu Glu Gly Lys Glu Gly Glu Asn Arg Ala Val Ile 130 135 140 His Tyr Arg Asp Asp Glu Thr Met Tyr Val Glu Ser Lys Lys Asp Arg 145 150 155 160 Val Thr Val Val Phe Ser Thr Val Phe Lys Asp Asp Asp Val Val 165 170 175 Ile Gly Lys Val Phe Met Gln Glu Phe Lys Glu Gly Arg Arg Ala Ser 180 185 190 His Thr Ala Pro Gln Val Leu Phe Ser His Arg Glu Pro Pro Leu Glu 195 200 205 Leu Lys Asp Thr Asp Ala Ala Val Gly Asp Asn Ile Gly Tyr Ile Thr Phe Val Leu Phe Pro Arg His Thr Asn Ala Ser Ala Arg Asp Asn Thr 225 230 235 240 Ile Asn Leu Ile His Thr Phe Arg Asp Tyr Leu His Tyr His Ile Lys Cys Ser Lys Ala Tyr Ile His Thr Arg Met Arg Ala Lys Thr Ser Asp 260 265 270 Phe Leu Lys Val Leu Asn Arg Ala Arg Pro Asp Ala Glu Lys Lys Glu 275 280 285 Met Lys Thr Ile Thr Gly Lys Thr Phe Ser Ser Arg

Met Ala Gly Ser Leu Pro Pro Cys Val Val Asp Cys Gly Thr Gly Tyr 1 10 15 Thr Lys Leu Gly Tyr Ala Gly Asn Thr Glu Pro Gln Phe Ile Ile Pro Ser Cys Ile Ala Ile Arg Glu Ser Ala Lys Val Val Asp Gln Ala Gln Arg Arg Val Leu Arg Gly Val Asp Asp Leu Asp Phe Phe Ile Gly Asp 50 60 Glu Ala Ile Asp Lys Pro Thr Tyr Ala Thr Lys Trp Pro Ile Arg His

<210> 134 <211> 418 <212> PRT <213> Home

<400> 134

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 65 70 75 80 Gly Ile Ile Glu Asp Trp Asp Leu Met Glu Arg Phe Met Glu Gln Val Val Phe Lys Tyr Leu Arg Ala Glu Pro Glu Asp His Tyr Phe Leu Met 100 105 110 Thr Glu Pro Pro Leu Asn Thr Pro Glu Asn Arg Glu Tyr Leu Ala Glu 115 120 125 Ile Met Phe Glu Ser Phe Asn Val Pro Gly Leu Tyr Ile Ala Val Gln 130 140 Ala Val Leu Ala Leu Ala Ala Ser Trp Thr Ser Arg Gln Val Gly Glu 145 150 160 Arg Thr Leu Thr Gly Ile Val Ile Asp Ser Gly Asp Gly Val Thr His $165 \hspace{1.5cm} 170 \hspace{1.5cm} 175$ Val Ile Pro Val Ala Glu Gly Tyr Val Ile Gly Ser Cys Ile Lys His 180 185 190 Ile Pro Ile Ala Gly Arg Asp Ile Thr Tyr Phe Ile Gln Gln Leu Leu 195 200 205 Arg Glu Arg Glu Val Gly Ile Pro Pro Glu Gln Ser Leu Glu Thr Ala 210 215 220Lys Ala Ile Lys Glu Lys Tyr Cys Tyr Ile Cys Pro Asp Ile Val Lys Glu Phe Ala Lys Tyr Asp Val Asp Pro Arg Lys Trp Ile Lys Gln Tyr 245 250 255 Thr Gly Ile Asn Ala Ile Asn Gln Lys Lys Phe Val Ile Asp Val Gly 260 265 270 Tyr Glu Arg Phe Leu Gly Pro Glu Ile Phe Phe His Pro Glu Phe Ala 275 280 285 Asn Pro Asp Phe Met Glu Ser Ile Ser Asp Val Val Asp Glu Val Ile $290 \hspace{1cm} 295 \hspace{1cm} 300$ Gln Asn Cys Pro Ile Asp Val Arg Arg Pro Leu Tyr Lys Asn Val Val 305 310 315 Leu Ser Gly Gly Ser Thr Met Phe Arg Asp Phe Gly Arg Arg Leu Gln 325 330 335Arg Asp Leu Lys Arg Val Val Asp Ala Arg Leu Arg Leu Ser Glu Glu 340 345 350 Leu Ser Gly Gly Arg Ile Lys Pro Lys Pro Val Glu Val Gln Val Val 355 360 365 Thr His His Met Gln Arg Tyr Ala Val Trp Phe Gly Gly Ser Met Leu Ala Ser Thr Pro Glu Phe Phe Gln Val Cys His Thr Lys Lys Asp Tyr 385 390 395 400 Glu Glu Tyr Gly Pro Ser Ile Cys Arg His Asn Pro Val Phe Gly Val 405 410 415

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

135 1271 PRT

<213> Homo sapiens

Met Val Asp Pro Val Gly Phe Ala Glu Ala Trp Lys Ala Gln Phe Pro 1 10 15 Asp Ser Glu Pro Pro Arg Met Glu Leu Arg Ser Val Gly Asp Ile Glu Gln Glu Leu Glu Arg Cys Lys Ala Ser Ile Arg Arg Leu Glu Gln Glu 35 40 45 Val Asn Gln Glu Arg Phe Arg Met Ile Tyr Leu Gln Thr Leu Leu Ala $50 \hspace{1.5cm} 60$ Lys Glu Lys Lys Ser Tyr Asp Arg Gln Arg Trp Gly Phe Arg Arg Ala 65 70 75 . Ala Gln Ala Pro Asp Gly Ala Ser Glu Pro Arg Ala Ser Ala Ser Arg 85 90 95 Pro Gln Pro Ala Pro Ala Asp Gly Ala Asp Pro Pro Pro Ala Glu Glu 100 105 110 Pro Glu Ala Arg Pro Asp Gly Glu Gly Ser Pro Gly Lys Ala Arg Pro 115 120 125 Gly Thr Ala Arg Arg Pro Gly Ala Ala Ser Gly Glu Arg Asp Asp 130 140 Arg Gly Pro Pro Ala Ser Val Ala Ala Leu Arg Ser Asn Phe Glu Arg 145 150 155 160 Ile Arg Lys Gly His Gly Gln Pro Gly Ala Asp Ala Glu Lys Pro Phe 165 170 175 Tyr Val Asn Val Glu Phe His His Glu Arg Gly Leu Val Lys Val Asn 180 185 190 Asp Lys Glu Val Ser Asp Arg Ile Ser Ser Leu Gly Ser Gln Ala Met
195 200 205 Gln Met Glu Arg Lys Lys Ser Gln His Gly Ala Gly Ser Ser Val Gly 210 215 220 Asp Ala Ser Arg Pro Pro Tyr Arg Gly Arg Ser Ser Glu Ser Ser Cys 225 230 235 240 Gly Val Asp Gly Asp Tyr Glu Asp Ala Glu Leu Asn Pro Arg Phe Leu 245 250 255 Lys Asp Asn Leu Ile Asp Ala Asn Gly Gly Ser Arg Pro Pro Trp Pro 265 270 Pro Leu Glu Tyr Gln Pro Tyr Gln Ser Ile Tyr Val Gly Gly Met Met 275 280 285 Glu Gly Glu Gly Lys Gly Pro Leu Leu Arg Ser Gln Ser Thr Ser Glu 290 295 300

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln Glu Lys Arg Leu Thr Trp Pro Arg Arg Ser Tyr Ser Pro Arg Ser 305 310 315 Phe Glu Asp Cys Gly Gly Gly Tyr Thr Pro Asp Cys Ser Ser Asn Glu Asn Leu Thr Ser Ser Glu Glu Asp Phe Ser Ser Gly Gln Ser Ser Arg 340 345 350 Val Ser Pro Ser Pro Thr Thr Tyr Arg Met Phe Arg Asp Lys Ser Arg Ser Pro Ser Gln Asn Ser Gln Gln Ser Phe Asp Ser Ser Ser Pro Pro 370 380 Thr Pro Gln Cys His Lys Arg His Arg His Cys Pro Val Val Val Ser 385 390 395 400 Glu Ala Thr Ile Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn 405 410 415 Asp Gly Glu Gly Ala Phe His Gly Asp Ala Asp Gly Ser Phe Gly Thr 420 430 Pro Pro Gly Tyr Gly Cys Ala Ala Asp Arg Ala Glu Glu Gln Arg Arg 435 440 445 His Gln Asp Gly Leu Pro Tyr Ile Asp Asp Ser Pro Ser Ser Pro 450 460 His Leu Ser Ser Lys Gly Arg Gly Ser Arg Asp Ala Leu Val Ser Gly 465 470 475 Ala Leu Glu Ser Thr Lys Ala Ser Glu Leu Asp Leu Glu Lys Gly Leu 485 490 495 Glu Met Arg Lys Trp Val Leu Ser Gly Ile Leu Ala Ser Glu Glu Thr 500 505 510 Tyr Leu Ser His Leu Glu Ala Leu Leu Leu Pro Met Lys Pro Leu Lys 515 520 525 Ala Ala Thr Thr Ser Gln Pro Val Leu Thr Ser Gln Gln Ile Glu 530 535 540 Thr Ile Phe Phe Lys Val Pro Glu Leu Tyr Glu Ile His Lys Glu Phe 545 550 555 560 Tyr Asp Gly Leu Phe Pro Arg Val Gln Gln Trp Ser His Gln Gln Arg 565 570 575 val Gly Asp Leu Phe Gln Lys Leu Ala Ser Gln Leu Gly Val Tyr Arg 580 585 590 Ala Phe Val Asp Asn Tyr Gly Val Ala Met Glu Met Ala Glu Lys Cys 595 600 605 Cys Gln Ala Asn Ala Gln Phe Ala Glu Ile Ser Glu Asn Leu Arg Ala 610 615 620 Arg Ser Asn Lys Asp Ala Lys Asp Pro Thr Thr Lys Asn Ser Leu Glu 625 630 635

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Leu Leu Tyr Lys Pro Val Asp Arg Val Thr Arg Ser Thr Leu Val 645 650 655

Leu His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro 660 665 670 Leu Leu Gln Asp Ala Leu Arg Ile Ser Gln Asn Phe Leu Ser Ser Ile 675 680 685 Asn Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly Glu His Arg Gln Leu Leu Lys Asp Ser Phe Met Val Glu Leu Val Glu 705 710 715 720 Gly Ala Arg Lys Leu Arg His Val Phe Leu Phe Thr Glu Leu Leu Leu 735 Cys Thr Lys Leu Lys Lys Gln Ser Gly Gly Lys Thr Gln Gln Tyr Asp 740 745 750 Cys Lys Trp Tyr Ile Pro Leu Thr Asp Leu Ser Phe Gln Met Val Asp $755 \hspace{1.5cm} 760 \hspace{1.5cm} 765$ Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val Pro Asp Glu Glu Leu Asp Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys Ser Asp Ile Gln Arg Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys 805 810 815 Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Leu Met Ser Pro Ser Met $820 \hspace{1.5cm} 825 \hspace{1.5cm} 830$ Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile 835 840 845 Ser Ser Asp Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln 850 860 Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln 865 870 875 880 Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro 885 890 895 Leu Thr Ile Asn Lys Glu Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe 900 910 Leu Asn Val Ile Val His Ser Ala Thr Gly Phe Lys Gln Ser Ser Asn 915 920 925 Leu Tyr Cys Thr Leu Glu Val Asp Ser Phe Gly Tyr Phe Val Asn Lys 930 935 940Ala Lys Thr Arg Val Tyr Arg Asp Thr Ala Glu Pro Asn Trp Asn Glu 945 950 955 960 Glu Phe Glu Ile Glu Leu Glu Gly Ser Gln Thr Leu Arg Ile Leu Cys Tyr Glu Lys Cys Tyr Asn Lys Thr Lys Ile Pro Lys Glu Asp Gly Glu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ser Thr Asp Arg Leu Met Gly Lys Gly Gln Val Gln Leu Asp Pro Gln
995

Ala Leu Gln Asp Arg Asp Trp Gln Arg Thr Val Ile Ala Met Asn
1010
1015

Gly Ile Glu Val Lys Leu Ser Val Lys Phe Asn Ser Arg Glu Phe 1025 1030

Ser Leu Lys Arg Met Pro Ser Arg Lys Gln Thr Gly Val Phe Gly 1040 1050

Val Lys Ile Ala Val Val Thr Lys Arg Glu Arg Ser Lys Val Pro $1055 \hspace{1.5cm} 1060 \hspace{1.5cm} 1065$

Tyr Ile Val Arg Gln Cys Val Glu Glu Ile Glu Arg Arg Gly Met 1070 1080

Glu Glu Val Gly Ile Tyr Arg Val Ser Gly Val Ala Thr Asp Ile 1085 1090 1095

Gln Ala Leu Lys Ala Ala Phe Asp Val Asn Asn Lys Asp Val Ser 1100 1110

Val Met Met Ser Glu Met Asp Val Asn Ala Ile Ala Gly Thr Leu 1115 1120 1125

Lys Leu Tyr Phe Arg Glu Leu Pro Glu Pro Leu Phe Thr Asp Glu 1130 1140

Phe Tyr Pro Asn Phe Ala Glu Gly Ile Ala Leu Ser Asp Pro Val 1145 1150 1155

Ala Lys Glu Ser Cys Met Leu Asn Leu Leu Leu Ser Leu Pro Glu 1160 1165 1170

Ala Asn Leu Leu Thr Phe Leu Phe Leu Leu Asp His Leu Lys Arg 1175 1180 1185

Val Ala Glu Lys Glu Ala Val Asn Lys Met Ser Leu His Asn Leu 1190 1200

Ala Thr Val Phe Gly Pro Thr Leu Leu Arg Pro Ser Glu Lys Glu 1205 1215

Ser Lys Leu Pro Ala Asn Pro Ser Gln Pro Ile Thr Met Thr Asp 1220 1225 1230

Ser Trp Ser Leu Glu Val Met Ser Gln Val Gln Val Leu Leu Tyr 1235 1240 1245

Phe Leu Gln Leu Glu Ala Ile Pro Ala Pro Asp Ser Lys Arg Gln 1250 1260

Ser Ile Leu Phe Ser Thr Glu Val

<210> 136

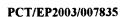
<2115 122 <212> PRT

<213> Homo sapiens

<400> 136

Met Val Asp Pro Val Gly Phe Ala Glu Ala Trp Lys Ala Gln Phe Pro

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asp Ser Glu Pro Pro Arg Met Glu Leu Arg Ser Val Gly Asp Ile Glu Gln Glu Leu Glu Arg Cys Lys Ala Ser Ile Arg Arg Leu Glu Gln Glu 35 40 45 Val Asn Gln Glu Arg Phe Arg Met Ile Tyr Leu Gln Thr Leu Leu Ala 50 55 60 Lys Glu Lys Lys Ser Tyr Asp Arg Gln Arg Trp Gly Phe Arg Arg Ala 65 70 80 Ala Gln Ala Pro Asp Gly Ala Ser Glu Pro Arg Ala Ser Ala Ser Arg 90 95 Pro Gln Pro Ala Pro Ala Asp Gly Ala Asp Pro Pro Pro Ala Glu Glu 100 105 110 Pro Glu Ala Arg Pro Asp Gly Glu Gly Ser Pro Gly Lys Ala Arg Pro 115 120 125 Gly Thr Ala Arg Arg Pro Gly Ala Ala Ser Gly Glu Arg Asp Asp 130 140 Arg Gly Pro Pro Ala Ser Val Ala Ala Leu Arg Ser Asn Phe Glu Arg 145 150 155 160 Ile Arg Lys Gly His Gly Gln Pro Gly Ala Asp Ala Glu Lys Pro Phe 165 170 175 Tyr Val Asn Val Glu Phe His His Glu Arg Gly Leu Val Lys Val Asn 180 185 190 Asp Lys Glu Val Ser Asp Arg Ile Ser Ser Leu Gly Ser Gln Ala Met 195 200 205 Gln Met Glu Arg Lys Lys Ser Gln His Gly Ala Gly Ser Ser Val Gly 210 220 Asp Ala Ser Arg Pro Pro Tyr Arg Gly Arg Ser Ser Glu Ser Ser Cys 225 230 235 240 Gly Val Asp Gly Asp Tyr Glu Asp Ala Glu Leu Asn Pro Arg Phe Leu 245 250 Lys Asp Asn Leu Ile Asp Ala Asn Gly Gly Ser Arg Pro Pro Trp Pro 260 265 270Pro Leu Glu Tyr Gln Pro Tyr Gln Ser Ile Tyr Val Gly Gly Ile Met $275 \hspace{1cm} 280 \hspace{1cm} 285$ Glu Gly Glu Gly Lys Gly Pro Leu Leu Arg Ser Gln Ser Thr Ser Glu 290 295 300Gln Glu Lys Arg Leu Thr Trp Pro Arg Arg Ser Tyr Ser Pro Arg Ser 305 310 320 Phe Glu Asp Cys Gly Gly Gly Tyr Thr Pro Asp Cys Ser Ser Asn Glu Asn Leu Thr Ser Ser Glu Glu Asp Phe Ser Ser Gly Gln Ser Ser Arg



Protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Val Ser Pro Ser Pro Thr Thr Tyr Arg Met Phe Arg Asp Lys Ser Arg Ser Pro Ser Gln Asn Ser Gln Gln Ser Phe Asp Ser Ser Ser Pro Pro Thr Pro Gln Cys His Lys Arg His Arg His Cys Pro Val Val Ser 385 390 395 400 Glu Ala Thr Ile Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn 405 410 415 Asp Asp Glu Gly Ala Phe His Gly Asp Ala Asp Gly Ser Phe Gly Thr 420 430 Pro Pro Gly Tyr Gly Cys Ala Ala Asp Arg Ala Glu Glu Gln Arg Arg 435 440 His Gln Asp Gly Leu Pro Tyr Ile Asp Asp Ser Pro Ser Ser Pro 450 455 460 His Leu Ser Ser Lys Gly Arg Gly Ser Arg Asp Ala Leu Val Ser Gly 465 470 475 480 Ala Leu Lys Ser Thr Lys Ala Ser Glu Leu Asp Leu Glu Lys Gly Leu 495 Glu Met Arg Lys Trp Val Leu Ser Gly Ile Leu Ala Ser Glu Glu Thr 500 505 510 Tyr Leu Ser His Leu Glu Ala Leu Leu Leu Pro Met Lys Pro Leu Lys 515 520 525 Ala Ala Thr Thr Ser Gln Pro Val Leu Thr Ser Gln Gln Ile Glu 530 535 540 Thr Ile Phe Phe Lys Val Pro Glu Leu Tyr Glu Ile His Lys Glu Ser 545 550 555 Tyr Asp Gly Leu Phe Pro Arg Val Gln Gln Trp Ser His Gln Gln Arg 565 570 575 Val Gly Asp Leu Phe Gln Lys Leu Ala Ser Gln Leu Gly Val Tyr Arg 580 585 590 Ala Phe Val Asp Asn Tyr Gly Val Ala Met Glu Met Ala Glu Lys Cys 595 600 605 Cys Gln Ala Asn Ala Gln Phe Ala Glu Ile Ser Glu Asn Leu Arg Ala 610 615 620 Arg Ser Asn Lys Asp Ala Lys Asp Pro Thr Thr Lys Asn Ser Leu Glu 625 630 635 Thr Leu Leu Tyr Lys Pro Val Asp Arg Val Thr Arg Ser Thr Leu Val Leu His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro Leu Leu Gln Asp Ala Leu Arg Ile Ser Gln Asn Phe Leu Ser Ser Ile
675 680 685 Asn Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 690 695 700 Glu His Arg Gln Leu Leu Lys Asp Ser Phe Met Val Glu Leu Val Glu 705 710 715 720 Gly Ala Arg Lys Leu Arg His Val Phe Leu Phe Thr Asp Leu Leu Leu 735 Cys Thr Lys Leu Lys Lys Gln Ser Gly Gly Lys Thr Gln Gln Tyr Asp 740 745 750 Cys Lys Trp Tyr Ile Pro Leu Thr Asp Leu Ser Phe Gln Met Val Asp $755 \hspace{1.5cm} 765 \hspace{1.5cm} 765$ Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val Pro Asp Glu Glu Leu Asp Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys Ser Asp Ile Gln Arg Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys 805 810 815 Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Leu Met Ser Pro Ser Met 820 825 830 Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile 835 840 845 Ser Ser Asp Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln 850 860 Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln .865 870 875 880 Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro 885 890 895 Leu Thr Ile Asn Lys Glu Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe $900 \hspace{0.5in} 910$ Leu Asn Val Ile Val His Ser Ala Thr Gly Phe Lys Gln Ser Ser Asn 915 920 925 Leu Tyr Cys Thr Leu Glu Val Asp Ser Phe Gly Tyr Phe Val Asn Lys 930 940 Ala Lys Thr Arg Val Tyr Arg Asp Thr Ala Glu Pro Asn Trp Asn Glu 945 950 955 960 Leu Asp Pro Gln Ala Leu Gln Asp Arg Asp Trp Gln Arg Thr Val Ile 965 970 975 Ala Met Asn Gly Ile Glu Val Lys Leu Ser Val Lys Phe Asn Ser Arg 980 985 990Glu Phe Ser Leu Lys Arg Met Pro Ser Arg Lys Gln Thr Gly Val Phe 995 1000 1005 Gly Val Lys Ile Ala Val Val Thr Lys Arg Glu Arg Ser Lys Val 1010 $1020\,$ Pro Tyr Ile Val Arg Gln Cys Val Glu Glu Ile Glu Arg Arg Gly

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Met Glu Glu Val Gly Ile Tyr Arg Val Ser Gly Val Ala Thr Asp
1040 1045 1050

Ile Gln Ala Leu Lys Ala Ala Phe Asp Val Asn Asn Lys Asp Val 1055 1065

WO 2004/009622

Ser Val Met Met Ser Glu Met Asp Val Asn Ala Ile Ala Gly Thr $1070 \hspace{1.5cm} 1080$

Leu Lys Leu Tyr Phe Arg Glu Leu Pro Glu Pro Leu Phe Thr Asp 1085 1095

Glu Phe Tyr Pro Asn Phe Ala Glu Gly Ile Ala Leu Ser Asp Pro 1100 1110

Val Ala Lys Glu Ser Cys Met Leu Asn Leu Leu Leu Ser Leu Pro 1115 1120 1125

Glu Ala Asn Leu Leu Thr Phe Leu Phe Leu Leu Asp His Leu Lys 1130 1140

Arg Val Ala Glu Lys Glu Ala Val Asn Lys Met Ser Leu His Asn 1145 1150 1155

Leu Ala Thr Val Phe Gly Pro Thr Leu Leu Arg Pro Ser Glu Lys 1160 1165 1170

Glu Ser Lys Leu Pro Ala Asn Pro Ser Gln Pro Ile Thr Met Thr 1175 1180 1185

Asp Ser Trp Ser Leu Glu Val Met Ser Gln Val Gln Val Leu Leu 1190 1200

Tyr Phe Leu Gln Leu Glu Ala Ile Pro Ala Pro Asp Ser Lys Arg 1205 1210 1215

Gln Ser Ile Leu Phe Ser Thr Glu Val 1220

<21U> 13/

<211> 304

<213> Homo sapiens

<400> 137

Met Ala Gly Asn Phe Asp Ser Glu Glu Arg Ser Ser Trp Tyr Trp Gly $1 ext{0} ext{1}$

Arg Leu Ser Arg Gln Glu Ala Val Ala Leu Leu Gln Gly Gln Arg His $20 \hspace{1cm} 30$

Leu Ser Val Ser Glu Asn Ser Arg Val Ser His Tyr Ile Ile Asn Ser 50 60

Ser Gly Pro Arg Pro Pro Val Pro Pro Ser Pro Ala Gln Pro Pro 65 70 75 80

Gly Val Ser Pro Ser Arg Leu Arg Ile Gly Asp Gln Glu Phe Asp Ser 85 90 95

Leu pro Ala Leu Leu Glu phe Tyr Lys Ile His Tyr Trp Asp Thr Thr $100 \hspace{1cm} 105 \hspace{1cm} 110$

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Leu Ile Glu Pro Val Ser Arg Ser Arg Gln Gly Ser Gly Val Ile Leu Arg Gln Glu Glu Ala Glu Tyr Val Arg Ala Leu Phe Asp Phe Asn 130 140 Gly Asn Asp Glu Glu Asp Leu Pro Phe Lys Lys Gly Asp Ile Leu Arg 145 150 155 160 Ile Arg Asp Lys Pro Glu Glu Gln Trp Trp Asn Ala Glu Asp Ser Glu 165 170 175 Gly Lys Arg Gly Met Ile Pro Val Pro Tyr Val Glu Lys Tyr Arg Pro 180 185 190 Ala Ser Ala Ser Val Ser Ala Leu Ile Gly Gly Asn Gln Glu Gly Ser 195 200 205 His Pro Gln Pro Leu Gly Pro Pro Glu Pro Gly Pro Tyr Ala Gln Pro 210 215 220 Ser Val Asn Thr Pro Leu Pro Asn Leu Gln Asn Gly Pro Ile Tyr Ala 225 230 235 240 Arg Val Ile Gln Lys Arg Val Pro Asn Ala Tyr Asp Lys Thr Ala Leu 245 250 255 Ala Leu Glu Val Gly Glu Leu Val Lys Val Thr Lys Ile Asn Val Ser 260 265 270 Gly Gln Trp Glu Gly Gly Cys Asn Gly Lys Arg Gly His Phe Pro Phe 275 280 285 Thr His Val Arg Leu Leu Asp Gln Gln Asn Pro Asp Glu Asp Phe Ser

Met Ala Ala Ala Ala Ala Gly Ala Gly Pro Glu Met Val Arg Gly $1 \ \ \, 10 \ \ \, 15$ Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly 20 25 30 Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Val Asn Lys 35 40 45Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr $50 \hspace{1cm} 55$ Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His 65 70 75 80 Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu 90 95 Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu 100 105 110 Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr

¹³⁸ 360 PRT

Homo sapiens

<400> 138



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr 145 150 160 Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro 165 170 175 Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp $180 \hspace{1cm} 185 \hspace{1cm} 190$ Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser 195 200 205 Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn 210 220 Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile 225 230 235 240 Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile 245 250 255Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys 260 265 270 Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val 290 295 300 Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser 305 310 315 320 Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp 325 330 335 Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala 340 345 Arg Phe Gln Pro Gly Tyr Arg Ser

<210> 139 <211> 694 <212> PRT <213> Homo sapiens

Met Ser Gly Gly Glu Val Val Cys Ser Gly Trp Leu Arg Lys Ser Pro 1 10 15 Pro Glu Lys Leu Lys Arg Tyr Ala Trp Lys Arg Arg Trp Phe Val Leu Arg Ser Gly Arg Leu Thr Gly Asp Pro Asp Val Leu Glu Tyr Tyr 40 45Lys Asn Asp His Ala Lys Lys Pro Ile Arg Ile Ile Asp Leu Asn Leu 50 60 Protein Complexes of cellular networks underlying the development of cancer and other diseases.5T25.txt
Cys Gln Gln Val Asp Ala Gly Leu Thr Phe Asn Lys Lys Glu Phe Glu
65 70 75 80

Asn Ser Tyr Ile Phe Asp Ile Asn Thr Ile Asp Arg Ile Phe Tyr Leu 85 90 95 Val Ala Asp Ser Glu Glu Met Asn Lys Trp Val Arg Cys Ile Cys 100 105 Asp Ile Cys Gly Phe Asn Pro Thr Glu Glu Asp Pro Val Lys Pro Pro 115 120 125 Gly Ser Ser Leu Gln Ala Pro Ala Asp Leu Pro Leu Ala Ile Asn Thr 130 135 140 Ala Pro Pro Ser Thr Gln Ala Asp Ser Ser Ser Ala Thr Leu Pro Pro 145 150 155 160 Pro Tyr Gln Leu Ile Asn Val Pro Pro His Leu Glu Thr Leu Gly Ile 165 170 175 Gln Glu Asp Pro Gln Asp Tyr Leu Leu Leu Ile Asn Cys Gln Ser Lys 180 185 190 Lys Pro Glu Pro Thr Arg Thr His Ala Asp Ser Gly Lys Ser Thr Ser 195 200 205 Ser Glu Thr Asp Ser Asn Asp Asn Val Pro Ser His Lys Asn Pro Ala Ser Ser Gln Ser Lys His Gly Met Asn Gly Phe Phe Gln Gln Met 225 230 235 240 Ile Tyr Asp Ser Pro Pro Ser Arg Ala Pro Ser Ala Ser Val Asp Ser 250 255 Ser Leu Tyr Asn Leu Pro Arg Ser Tyr Ser His Asp Val Leu Pro Lys Val Ser Pro Ser Ser Thr Glu Ala Asp Gly Glu Leu Tyr Val Phe Asn 275 280 285 Thr Pro Ser Gly Thr Ser Ser Val Glu Thr Gln Met Arg His Val Ser 290 295 300 Ile Ser Tyr Asp Ile Pro Pro Thr Pro Gly Asn Thr Tyr Gln Ile Pro 305 310 315 320 Arg Thr Phe Pro Glu Gly Thr Leu Gly Gln Thr Ser Lys Leu Asp Thr 325 330 335 Ile Pro Asp Ile Pro Pro Pro Arg Pro Pro Lys Pro His Pro Ala His 340 345 350 Asp Arg Ser Pro Val Glu Thr Cys Ser Ile Pro Arg Thr Ala Ser Asp 365 366 Thr Asp Ser Ser Tyr Cys Ile Pro Thr Ala Gly Met Ser Pro Ser Arg Ser Asn Thr Ile Ser Thr Val Asp Leu Asn Lys Leu Arg Lys Asp Ala Ser Ser Gln Asp Cys Tyr Asp Ile Pro Arg Ala Phe Pro Ser Asp Arg 415 415



Protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Ser Ser Ser Leu Glu Gly Phe His Asn His Phe Lys Val Lys Asn Val 420 425 430 Leu Thr Val Gly Ser Val Ser Ser Glu Glu Leu Asp Glu Asn Tyr Val 435 440 445 Pro Met Asn Pro Asn Ser Pro Pro Arg Gln His Ser Ser Ser Phe Thr 450 455 460 Glu Pro Ile Gln Glu Ala Asn Tyr Val Pro Met Thr Pro Gly Thr Phe 465 470 475 480 Asp Phe Ser Ser Phe Gly Met Gln Val Pro Pro Pro Ala His Met Gly 485 490 495 Phe Arg Ser Ser Pro Lys Thr Pro Pro Arg Arg Pro Val Pro Val Ala Asp Cys Glu Pro Pro Pro Val Asp Arg Asn Leu Lys Pro Asp Arg Lys 515 525 Val Lys Pro Ala Pro Leu Glu Ile Lys Pro Leu Pro Glu Trp Glu Glu 530 535 540 Leu Gln Ala Pro Val Arg Ser Pro Ile Thr Arg Ser Phe Ala Arg Asp 545 555 560 Ser Ser Arg Phe Pro Met Ser Pro Arg Pro Asp Ser Val His Ser Thr 575 Thr Ser Ser Ser Asp Ser His Asp Ser Glu Glu Asn Tyr Val Pro Met 580 585 Asn Pro Asn Leu Ser Ser Glu Asp Pro Asn Leu Phe Gly Ser Asn Ser 595 600 605 Leu Asp Gly Gly Ser Ser Pro Met Ile Lys Pro Lys Gly Asp Lys Gln 610 620 Val Glu Tyr Leu Asp Leu Asp Leu Asp Ser Gly Lys Ser Thr Pro Pro 625 630 635 640 Arg Lys Gln Lys Ser Ser Gly Ser Gly Ser Ser Val Ala Asp Glu Arg 645 650 Val Asp Tyr Val Val Val Asp Gln Gln Lys Thr Leu Ala Leu Lys Ser 660 665 670 Thr Arg Glu Ala Trp Thr Asp Gly Arg Gln Ser Thr Glu Ser Glu Thr 675 680 / 685 Pro Ala Lys Ser Val Lys 690

<210> 140 <211> 284 <212> PRT

<400> 140

Met Asp Ser Tyr Ser Thr Tyr Leu Ala Thr val Lys Val Ser Gly Ser 10 10

Trp Leu Glu Glu Gln Asp Glu Asp Ile Tyr Glu Ala Glu Ser Arg val

<212> PKI <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt $\frac{20}{20}$

Pro Leu Pro His Pro Phe Pro Leu Cys Glu His Leu Asp Glu Asn Asn $35 \hspace{1cm} 40 \hspace{1cm} 45$ Ser Val Ile Val Asn Thr Ser Ile Phe His Phe Ile His Lys Arg Asn 50 60 Gly His Ile Leu Lys Leu Ile Ser Lys Ile Ser Leu Pro Thr Pro Pro 65 70 75 80 Tyr Ser Leu Glu His Ala Lys Val Thr Gln Thr Glu Leu Met Arg Glu 85 90 95 Ser Phe Arg Gln Lys Gln Glu Ala Thr Glu Ser Leu Lys Cys Gln Glu Glu Leu Arg Glu Arg Leu His Glu Glu Ser Arg Ala Arg Glu Gln Leu 115 120 125 Ala Val Glu Leu Ser Lys Ala Glu Gly Val Ile Asp Gly Tyr Ala Asp 130 140 Glu Lys Thr Leu Phe Glu Arg Gln Ile Gln Glu Lys Thr Asp Ile Ile 145 150 155 160 Asp Arg Leu Glu Glu Leu Leu Cys Ala Ser Asn Arg Leu Gln Glu 165 170 175 Leu Glu Ala Glu Gln Gln Gln Ile Gln Glu Glu Arg Glu Leu Leu Ser 180 185 190 Arg Gln Lys Glu Ala Met Lys Ala Glu Ala Gly Pro Val Glu Gln Gln 195 200 205 Leu Leu Gln Glu Thr Glu Lys Leu Met Lys Glu Lys Leu Glu Val Gln Cys Gln Ala Glu Lys Val Arg Asp Asp Leu Gln Lys Gln Val Lys Ala 225 230 235 240 Leu Glu Ile Asp Val Glu Glu Gln Val Ser Arg Phe Ile Glu Leu Glu 245 250 255 Gln Glu Lys Asn Thr Glu Leu Met Asp Leu Arg Gln Gln Asn Gln Ala 260 265 270 Leu Glu Lys Gln Leu Glu Lys Lys Lys Lys Lys Lys Lys

Met Ala Ser Ala Cys Gly Ala Pro Gly Pro Gly Gly Ala Leu Gly Ser Gln Ala Pro Ser Trp Tyr His Arg Asp Leu Ser Arg Ala Ala Ala Glu Glu Leu Leu Ala Arg Ala Gly Arg Asp Gly Ser Phe Leu Val Arg Asp

<210> 141 <211> 1258 <212> PRT <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ser Glu Ser Val Ala Gly Ala Phe Ala Leu Cys Val Leu Tyr Gln Lys
50 55 60

His Val His Thr Tyr Arg Ile Leu Pro Asp Gly Glu Asp Phe Leu Ala Val Gln Thr Ser Gln Gly Val Pro Val Arg Arg Phe Gln Thr Leu Gly 90 95 Glu Leu Ile Gly Leu Tyr Ala Gln Pro Asn Gln Gly Leu Val Cys Ala 100 105 110 Leu Leu Pro Val Glu Gly Glu Arg Glu Pro Asp Pro Pro Asp Asp 115 120 125 Arg Asp Ala Ser Asp Gly Glu Asp Glu Lys Pro Pro Leu Pro Pro Arg 130 135 140 Ser Gly Ser Thr Ser Ile Ser Ala Pro Thr Gly Pro Ser Ser Pro Leu 145 150 155 160 Pro Ala Pro Glu Thr Pro Thr Ala Pro Ala Ala Glu Ser Ala Pro Asn 165 170 175 Gly Leu Ser Thr Val Ser His Asp Tyr Leu Lys Gly Ser Tyr Gly Leu 180 185 190 Asp Leu Glu Ala Val Arg Gly Gly Ala Ser His Leu Pro His Leu Thr Arg Thr Leu Ala Thr Ser Cys Arg Arg Leu His Ser Glu Val Asp Lys Val Leu Ser Gly Leu Glu Ile Leu Ser Lys Val Phe Asp Gln Gln Ser 225 230 240 Ser Pro Met Val Thr Arg Leu Leu Gln Gln Gln Asn Leu Pro Gln Thr Gly Glu Gln Glu Leu Glu Ser Leu Val Leu Lys Leu Ser Val Leu Lys 260 265 270Asp Phe Leu Ser Gly Ile Gln Lys Lys Ala Leu Lys Ala Leu Gln Asp 275 280 285Met Ser Ser Thr Ala Pro Pro Ala Pro Gln Pro Ser Thr Arg Lys Ala 290 300 Lys Thr Ile Pro Val Gln Ala Phe Glu Val Lys Leu Asp Val Thr Leu 305 310 315 Gly Asp Leu Thr Lys Ile Gly Lys Ser Gln Lys Phe Thr Leu Ser Val 325 330 335 Asp Val Glu Gly Gly Arg Leu Val Leu Leu Arg Arg Gln Arg Asp Ser 340 345 Gln Glu Asp Trp Thr Thr Phe Thr His Asp Arg Ile Arg Gln Leu Ile 355 360 365 Lys Ser Gln Arg Val Gln Asn Lys Leu Gly Val Val Phe Glu Lys Glu Lys Asp Arg Thr Gln Arg Lys Asp Phe Ile Phe Val Ser Ala Arg Lys 385 390 395

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Glu Ala Phe Cys Gln Leu Leu Gln Leu Met Lys Asn Lys His Ser Lys Gln Asp Glu Pro Asp Met Ile Ser Val Phe Ile Gly Thr Trp Asn Met Gly Ser Val Pro Pro Pro Lys Asn Val Thr Ser Trp Phe Thr Ser Lys Gly Leu Gly Lys Thr Leu Asp Glu Val Thr Val Thr Ile Pro His $450 \hspace{1cm} 455$ Asp Ile Tyr Val Phe Gly Thr Gln Glu Asn Ser Val Gly Asp Arg Glu 465 470 475Trp Leu Asp Leu Leu Arg Gly Gly Leu Lys Glu Leu Thr Asp Leu Asp Tyr Arg Pro Ile Ala Met Gln Ser Leu Trp Asn Ile Lys Val Ala Val 500 505 510 Leu Val Lys Pro Glu His Glu Asn Arg Ile Ser His Val Ser Thr Ser 515 520 525 Ser Val Lys Thr Gly Ile Ala Asn Thr Leu Gly Asn Lys Gly Ala Val 530 540 Gly Val Ser Phe Met Phe Asn Gly Thr Ser Phe Gly Phe Val Asn Cys 545 550 555His Leu Thr Ser Gly Asn Glu Lys Thr Ala Arg Arg Asn Gln Asn Tyr 565 570 575 Leu Asp Ile Leu Arg Leu Leu Ser Leu Gly Asp Arg Gln Leu Asn Ala 580 585 590 Phe Asp Ile Ser Leu Arg Phe Thr His Leu Phe Trp Phe Gly Asp Leu 595 600 605Asn Tyr Arg Leu Asp Met Asp Ile Gln Glu Ile Leu Asn Tyr Ile Ser 610 620 Arg Lys Glu Phe Glu Pro Leu Leu Arg Val Asp Gln Leu Asn Leu Glu 625 630 635 Arg Glu Lys His Lys Val Phe Leu Arg Phe Ser Glu Glu Glu Ile Ser 645 650 655 Phe Pro Pro Thr Tyr Arg Tyr Glu Arg Gly Ser Arg Asp Thr Tyr Ala 660 665 670 Trp His Lys Gln Lys Pro Thr Gly Val Arg Thr Asn Val Pro Ser Trp 675 680 685Cys Asp Arg Ile Leu Trp Lys Ser Tyr Pro Glu Thr His Ile Ile Cys 690 700Asn Ser Tyr Gly Cys Thr Asp Asp Ile Val Thr Ser Asp His Ser Pro Val Phe Gly Thr Phe Glu Val Gly Val Thr Ser Gln Phe Ile Ser Lys 725 730 735

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Lys Gly Leu Ser Lys Thr Ser Asp Gln Ala Tyr Ile Glu Phe Glu Ser
740 745 750

Ile Glu Ala Ile Val Lys Thr Ala Ser Arg Thr Lys Phe Phe Ile Glu Phe Tyr Ser Thr Cys Leu Glu Glu Tyr Lys Lys Ser Phe Glu Asn Asp Ala Gln Ser Ser Asp Asn Ile Asn Phe Leu Lys Val Gln Trp Ser Ser 785 790 795 800 Arg Gln Leu Pro Thr Leu Lys Pro Ile Leu Ala Asp Ile Glu Tyr Leu 805 810 815 Gln Asp Gln His Leu Leu Leu Thr Val Lys Ser Met Asp Gly Tyr Glu 820 . 825 830 Ser Tyr Gly Glu Cys Val Val Ala Leu Lys Ser Met Ile Gly Ser Thr 835 840 845 Ala Gln Gln Phe Leu Thr Phe Leu Ser His Arg Gly Glu Glu Thr Gly 850 860 Asn Ile Arg Gly Ser Met Lys Val Arg Val Pro Thr Glu Arg Leu Gly 865 870 875 880 Thr Arg Glu Arg Leu Tyr Glu Trp Ile Ser Ile Asp Lys Asp Glu Ala 885 890 895 Gly Ala Lys Ser Lys Ala Pro Ser Val Ser Arg Gly Ser Gln Glu Pro 900 905 910 Arg Ser Gly Ser Arg Lys Pro Ala Phe Thr Glu Ala Ser Cys Pro Leu 915 920 Ser Arg Leu Phe Glu Glu Pro Glu Lys Pro Pro Pro Thr Gly Arg Pro 930 935 940 Pro Ala Pro Pro Arg Ala Ala Pro Arg Glu Glu Pro Leu Thr Pro Arg 945 950 955 960 Leu Lys Pro Glu Gly Ala Pro Glu Pro Glu Gly Val Ala Ala Pro Pro 965 970 975 Pro Lys Asn Ser Phe Asn Asn Pro Ala Tyr Tyr Val Leu Glu Gly Val 980 985 990 Pro His Gln Leu Leu Pro Pro Glu Pro Pro Ser Pro Ala Arg Ala Pro 995 1000 1005 Val Pro Ser Ala Thr Lys Asn Lys Val Ala Ile Thr Val Pro Ala 1010 1015 1020 Pro Gln Leu Gly His His Arg His Pro Arg Val Gly Glu Gly Ser 1025 1030 1035 Ser Ser Asp Glu Glu Ser Gly Gly Thr Leu Pro Pro Pro Asp Phe 1040 1045 1050 Pro pro Pro Leu Pro Asp Ser Ala Ile Phe Leu Pro Pro Ser 1055 1060 1065 Leu ASP Pro Leu Pro Gly Pro Val Val Arg Gly Arg Gly Gly Ala 1070 1080

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Glu Ala Arg Gly Pro Pro Pro Pro Lys Ala His Pro Arg Pro Pro 1085 1090 1095

Leu Pro Pro Gly Pro Ser Pro Ala Ser Thr Phe Leu Gly Glu Val 1100 110

Gly Ser Gly Asp Asp Arg Ser Cys Ser Val Leu Gln Met Ala Lys

Thr Leu Ser Glu Val Asp Tyr Ala Pro Ala Gly Pro Ala Arg Ser 1130 1140

Ala Leu Leu Pro Gly Pro Leu Glu Leu Gln Pro Pro Arg Gly Leu 1145 1155

Pro Ser Asp Tyr Gly Arg Pro Leu Ser Phe Pro Pro Pro Arg Ile 1160 1170

Arg Glu Ser Ile Gln Glu Asp Leu Ala Glu Glu Ala Pro Cys Leu 1175 1180 1185

Gln Gly Gly Arg Ala Ser Gly Leu Gly Glu Ala Gly Met Ser Ala 1190 1200

Trp Leu Arg Ala Ile Gly Leu Glu Arg Tyr Glu Glu Gly Leu Val 1205 1210 1215

His Asn Gly Trp Asp Asp Leu Glu Phe Leu Ser Asp Ile Thr Glu 1220 1230

Glu Asp Leu Glu Glu Ala Gly Val Gln Asp Pro Ala His Lys Arg 1235 1240 1245

Leu Leu Asp Thr Leu Gln Leu Ser Lys 1250

<210> 142 <211> 1196 <212> PRT <213> Homo sapiens

<400> 142

Ala ASP ASP ASP Trp Trp Pro Met Gln Ile Leu Ile Lys Cys Pro Asn
1 10 15

Gln Ile Val Arg Gln Met Phe Gln Arg Leu Cys Ile His Val Ile Gln 20 25 30

Arg Leu Arg Pro Val His Ala His Leu Tyr Leu Gln Pro Gly Met Glu 35 40 45

Asp Gly Ser Asp Asp Met Asp Thr Ser Val Glu Asp Ile Gly Gly Arg

Ser Cys Val Thr Arg Phe Val Arg Thr Leu Leu Ile Met Glu His 65 70 75 80

Gly Val Lys Pro His Ser Lys His Leu Thr Glu Tyr Phe Ala Phe Leu 85 90 95

Tyr Glu Phe Ala Lys Met Gly Glu Glu Ser Gln Phe Leu Leu Ser

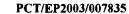
Leu Gln Ala Ile Ser Thr Met Val His Phe Tyr Met Gly Thr Lys Gly



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Pro Glu Asn Pro Gln Val Glu Val Leu Ser Glu Glu Glu Glu Glu Glu Glu Glu 130 Glu Glu Glu Glu Asp Ile Leu Ser Leu Ala Glu Glu Lys Tyr Arg 145 150 155 Pro Ala Ala Leu Glu Lys Met Ile Ala Leu Val Ala Leu Leu Val Glu 165 170 175 Gln Ser Arg Ser Glu Arg His Leu Thr Leu Ser Gln Thr Asp Met Ala 180 185 190 Ala Leu Thr Gly Gly Lys Gly Phe Pro Phe Leu Phe Gln His Ile Arg 195 200 205 Asp Gly Ile Asn Ile Arg Gln Thr Cys Asn Leu Ile Phe Ser Leu Cys 210 225 Arg Tyr Asn Asn Arg Leu Ala Glu His Ile Val Ser Met Leu Phe Thr 225 230 235 240 Ser Ile Ala Lys Leu Thr Pro Glu Ala Ala Asn Pro Phe Phe Lys Leu 245 250 255 Leu Thr Met Leu Met Glu Phe Ala Gly Gly Pro Pro Gly Met Pro Pro 260 265 270 Phe Ala Ser Tyr Ile Leu Gln Arg Ile Trp Glu Val Ile Glu Tyr Asn 275 280 285 Pro Ser Gln Cys Leu Asp Trp Leu Ala Val Gln Thr Pro Arg Asn Lys 290 295 300 Leu Ala His Ser Trp Val Leu Gln Asn Met Glu Asn Trp Val Glu Arg 305 310 315Phe Leu Leu Ala His Asn Tyr Pro Arg Val Arg Thr Ser Ala Ala Tyr 325 330 330Leu Leu Val Ser Leu Ile Pro Ser Asn Ser Phe Arg Gln Met Phe Arg 340 345Ser Thr Arg Ser Leu His Ile Pro Thr Arg Asp Leu Pro Leu Ser Pro 355 360 365 Asp Thr Thr Val Val Leu His Gln Val Tyr Asn Val Leu Leu Glý Leu 370 380 Leu Ser Arg Ala Lys Leu Tyr Val Asp Ala Ala Val His Gly Thr Thr 385 390 395 400 Lys Leu Val Pro Tyr Phe Ser Phe Met Thr Tyr Cys Leu Ile Ser Lys $405 \hspace{0.25cm} 410 \hspace{0.25cm} 415$ Thr Glu Lys Leu Met Phe Ser Thr Tyr Phe Met Asp Leu Trp Asn Leu 420 425 . 430Phe Gln Pro Lys Leu Ser Glu Pro Ala Ile Ala Thr Asn His Asn Lys 435 440 445 Gln Ala Leu Leu Ser Phe Trp Tyr Asn Val Cys Ala Asp Cys Pro Glu 450 455 460

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asn Ile Arg Leu Ile Val Gln Asn Pro Val Val Thr Lys Asn Ile Ala 465 470 475 480 Phe Asn Tyr Ile Leu Ala Asp His Asp Asp Gln Asp Val Val Leu Phe 485 490 495 Asn arg Gly Met Leu Pro Ala Tyr Tyr Gly Ile Leu Arg Leu Cys Cys 500 505Glu Gln Ser Pro Ala Phe Thr Arg Gln Leu Ala Ser His Gln Asn Ile 515 525 525 Gln Trp Ala Phe Lys Asn Leu Thr Pro His Ala Ser Gln Tyr Pro Gly 530 540 Ala Val Glu Glu Leu Phe Asn Leu Met Gln Leu Phe Ile Ala Gln Arg Pro Asp Met Arg Glu Glu Glu Leu Glu Asp Ile Lys Gln Phe Lys Lys
565 570 575 Thr Thr Ile Ser Cys Tyr Leu Arg Cys Leu Asp Gly Arg Ser Cys Trp Thr Thr Leu Ile Ser Ala Phe Arg Ile Leu Leu Glu Ser Asp Glu Asp Arg Leu Leu Val Val Phe Asn Arg Gly Leu Ile Leu Met Thr Glu Ser $610 \hspace{1.5cm} 620$ Phe Asn Thr Leu His Met Met Tyr His Glu Ala Thr Ala Cys His Val 625 630 635 640 Thr Gly Asp Leu Val Glu Leu Leu Ser Ile Phe Leu Ser Val Leu Lys 645 650 655 Ser Thr Arg Pro Tyr Leu Gln Arg Lys Asp Val Lys Gln Ala Leu Ile 660 670 Gln Trp Gln Glu Arg Ile Glu Phe Ala His Lys Leu Leu Thr Leu Leu 675 680 685 As n Ser Tyr Ser Pro Pro Glu Leu Arg Asn Ala Cys Ile Asp Val Leu $690 \hspace{1.5cm} 695 \hspace{1.5cm} 700$ Lys Glu Leu Val Leu Leu Ser Pro His Asp Phe Leu His Thr Leu Val 705 710 720 Pro Phe Leu Gln His Asn His Cys Thr Tyr His His Ser Asn Ile Pro 725 730 735 Met Ser Leu Gly Pro Tyr Phe Pro Cys Arg Glu Asn Ile Lys Leu Ile 740 745 750 Gly Gly Lys Ser Asn Ile Arg Pro Pro Arg Pro Glu Leu Asn Met Cys 755 760 765 Leu Leu Pro Thr Met Val Glu Thr Ser Lys Gly Lys Asp Asp Val Tyr ASP Arg Met Leu Leu ASP Tyr Phe Phe Ser Tyr His Gln Phe Ile His 785 790 795 800 Leu Leu Cys Arg Val Ala Ile Asn Cys Glu Lys Phe Thr Glu Thr Leu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 805 810

Val Lys Leu Ser Val Leu Val Ala Tyr Glu Gly Leu Pro Leu His Leu 820 825 830 Ala Leu Phe Pro Lys Leu Trp Thr Glu Leu Cys Gln Thr Gln Ser Ala 835 840 845Met Ser Lys Asn Cys Ile Lys Leu Leu Cys Glu Asp Pro Val Phe Ala 850 855 860 Glu Tyr Ile Lys Cys Ile Leu Met Asp Glu Arg Thr Phe Leu Asn Asn 865 870 880 Asn Ile Val Tyr Thr Phe Met Thr His Phe Leu Leu Lys Val Gln Ser 885 890 895 Gln Val Phe Ser Glu Ala Asn Cys Ala Asn Leu Ile Ser Thr Leu Ile 900 905 910 Thr Asn Leu Ile Ser Gln Tyr Gln Asn Leu Gln Ser Asp Phe Ser Asn 915 920 925 Arg Val Glu Ile Ser Lys Ala Ser Ala Ser Leu Asn Gly Asp Leu Arg 930 935 940 Ala Leu Ala Leu Leu Leu Ser Val His Thr Pro Lys Gln Leu Asn Pro 945 950 955 960 Ala Leu Ile Pro Thr Leu Gln Glu Leu Leu Ser Lys Cys Arg Thr Cys 965 970 975 Leu Gln Gln Arg Asn Ser Leu Gln Glu Gln Glu Ala Lys Glu Arg Lys 980 985 990 Thr Lys Asp Asp Glu Gly Ala Thr Pro Ile Lys Arg Arg Arg Val Ser 995 1000 Ser Asp Glu Glu His Thr Val Asp Ser Cys Ile Ser Asp Met Lys $1010 \hspace{1.5cm} 1020$ Thr Glu Thr Arg Glu Val Leu Thr Pro Thr Ser Thr Ser Asp Asn 1025 1030 1035 Glu Thr Arg Asp Ser Ser Ile Ile Asp Pro Gly Thr Glu Gln Asp 1040 1050 Leu Pro Ser Pro Glu Asn Ser Ser Val Lys Glu Tyr Arg Met Glu 1055 1065 Val Pro Ser Ser Phe Ser Glu Asp Met Ser Asn Ile Arg Ser Gln 1070 1080 His Ala Glu Glu Gln Ser Asn Asn Gly Arg Tyr Asp Asp Cys Lys Glu Phe Lys Asp Leu His Cys Ser Lys Asp Ser Thr Leu Ala Glu 1100 1110 1110 Glu Glu Ser Glu Phe Pro Ser Thr Ser Ile Ser Ala Val Leu Ser 1115 1120 1125 Asp Leu Ala Asp Leu Arg Ser Cys Asp Gly Gln Ala Leu Pro Ser

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Gln Asp Pro Glu Val Ala Leu Ser Leu Ser Cys Gly His Ser Arg

Gly Leu Phe Ser His Met Gln Gln His Asp Ile Leu Asp Thr Leu 1160 1170

Cys Arg Thr Ile Glu Ser Thr Ile His Val Val Thr Arg Ile Ser 1175 1180 1185

Gly Lys Gly Asn Gln Ala Ala Ser

<210> 143 <211> 1680 <212> PRT <213> Homo sapiens

<400> 143

Pro Gly Leu Val Gly Glu His Gly Gly His Cys Lys Val Leu Trp Leu 10 15

Ala Asn Ser Leu Tyr Ser Val Gly Leu Pro His His Ser His Gly Thr

Glu Pro Met Trp His Gly Asn His Val Gln Pro Gly Ala Thr His Arg.

Pro Asn Gln Gly Leu Glu Met Leu Gln Gly Leu Gly Ile Gly Met Lys 50 60

Ala Phe His Asn Phe Asn Tyr Phe Leu Phe Phe Tyr Asn Val Leu Leu 65 70 75 80

Gly Leu Gly Ala Cys Leu Ser Arg Leu Leu Ile Ser Cys Leu Leu Gly

Glu Gly Ala Asp Met Gly Phe Ser Ala Trp Ile Gly Met Leu Tyr Met 115 120 125

Asp His Tyr His Ile Asn Pro Val Leu Val Ser Phe Cys His Ile Leu 130 140

Ile Thr Asn His Arg Glu Lys Lys Leu Gln Gln Ser Thr Lys Tyr Trp 145 150 155 160

Cys Leu Asn Gln Ser Ala Glu Ser Leu Arg Ile Cys Ala Met Arg Gly 165 170 175

Gly Glu Asn Arg Pro Pro Ala Arg Val Gln Ser Ser Glu Glu Leu 180 185 190

Glu Leu Arg His Gln Ser Leu Asp Ala Phe Pro Gly Arg Arg Leu Pro 195 200 205

Gly Arg Gly Ile Gln Pro Ala Ala Lys Met Ser Ser Val Gly Lys Val 210 220

Thr Gln Val Pro Asn Gly Lys Ala Tyr Gln Gln Ile Phe Gln Ala Glu 225 230 235 240

Val Gln Leu Val His Ser Leu Ala Ala Thr Arg Lys Arg Ala Ala Glu 245 250 255

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Ser Val Thr Leu Lys Ser Gly Arg Ile Pro Met Met Lys Lys Val Glu Thr Pro Glu Gly Glu Val Met Ser Pro Arg Gln Gln Lys Trp Met 275 280 285 His Ser Leu Pro Asn Asp Trp Ile Met Glu Asn Pro Val Leu His Arg 290 295 300 Glu Lys Glu Arg Ala Lys Arg Glu Lys Ala Arg Glu Ser Glu Asn Thr 305 310 315 Ile Ala Ala Arg Glu Val Arg Gly Leu Met Asp Thr Ile Val Pro Glu 325 330 335 Lys Ile Ser Thr Ser Thr Phe Gln Arg Gln Ala Glu His Lys Arg Lys 340 345 350 Ser Tyr Glu Ser Ala Leu Ala Ser Phe Gln Glu Glu Ile Ala Gln Val 355 360 365 Gly Lys Glu Met Glu Pro Leu Ile Val Asp Thr Gly Gly Leu Phe Leu Lys Lys Leu Thr Glu Ser Asp Glu Glu Met Asn Arg Leu Phe Leu Lys 385 390 395 400 Val Glu Asn Asp Thr Asn Leu Glu Asp Tyr Thr Ile Gln Ala Leu Leu 405 410 415Glu Leu Trp Asp Lys Val Ala Gly Arg Leu Leu Arg Lys Gln Glu Ile Lys Glu Leu Asp Glu Ala Leu His Ser Leu Glu Phe Ser Arg Thr $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445$ Asp Lys Leu Lys Ser Val Leu Lys Lys Tyr Ala Glu Val Ile Glu Lys 450 460 Thr Ser Tyr Leu Met Arg Pro Glu Val Tyr Arg Leu Ile Asn Glu Glu 465 470 480 Ala Met Val Met Asn Tyr Ala Leu Leu Gly Asn Arg Lys Ala Leu Ala 485 490 495 Gln Leu Phe Val Asn Leu Met Glu Ser Thr Leu Gln Gln Glu Leu Asp 500 505 510 Ser Arg His Arg Trp Gln Gly Leu Val Asp Thr Trp Lys Ala Leu Lys 515 525 Lys Glu Ala Leu Leu Gln Ser Phe Ser Glu Phe Met Ala Ser Glu Ser 530 540 Ile His Thr Pro Pro Ala Val Thr Lys Glu Leu Glu Val Met Leu Lys 545 550 555 Thr Gln Asn Val Leu Gln Gln Arg Arg Leu Lys His Leu Cys Thr Ile 565 570 575 Cys Asp Leu Leu Pro Pro Ser Tyr Ser Lys Thr Gln Leu Thr Glu Trp

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Ser Ser Leu Asn Ser Leu Asn Lys Glu Leu Asp Thr Tyr His Val 595 600 605

Asp Cys Met Met Trp Ile Arg Leu Leu Tyr Glu Lys Thr Trp Gln Glu 610 620 Cys Leu Met His Val Gln Asn Cys Lys Lys Gln Leu Leu Asp Trp Lys 625 630 635 Ala Phe Thr Glu Glu Glu Ala Glu Thr Leu Val Asn Gln Phe Phe Phe 645 650 655 Gln Met Val Gly Ala Leu Gln Gly Lys Val Glu Glu Asp Leu Glu Leu 660 670 Leu Asp Lys Ser Phe Glu Thr Leu Ala Asp Gln Thr Glu Trp Gln Ser 675 680 685 Ser His Leu Phe Lys Tyr Phe Gln Glu Val Val Gln Leu Trp Glu Ala 690 695 700 His Gln Ser Glu Leu Leu Val Gln Glu Leu Glu Leu Glu Lys Arg Met 705 710 715 720 Glu Gln His Arg Gln Lys His Ser Leu Glu Ser Gln Val Gln Glu Ala 725 730 735 His Leu Asp Arg Leu Leu Asp Gln Leu Arg Gln Gln Ser Asp Lys Glu 745 750 Thr Leu Ala Phe His Leu Glu Lys Val Lys Asp Tyr Leu Lys Asn Met 755 760 765 Lys Ser Arg Tyr Glu Cys Phe His Thr Leu Leu Thr Lys Glu Val Met 770 780 Glu Tyr Pro Ala Ile Met Leu Lys Glu Leu Asn Ser Tyr Ser Ser Ala 785 790 795 800 Leu Ser Gln Tyr Phe Phe Val Arg Glu Ile Phe Glu Gln Asn Leu Ala 805 810 815 Gly Glu Val Ile Phe Lys Phe Arg Gln Pro Glu Ala His Glu Lys Pro 820 825 830 Ser Gln Lys Arg Val Lys Lys Leu Arg Lys Lys Gln Gly Ser Lys Glu .835 840 845 Asp Met Thr Arg Ser Glu Glu Ser Ile Ser Ser Gly Thr Ser Thr Ala 850 855 Arg Ser Val Glu Glu Val Glu Glu Glu Asn Asp Gln Glu Met Glu Ser 865 870 875 880 Phe Ile Thr Glu Glu Val Leu Gly Gln Gln Lys Lys Ser Pro Leu His 885 890 895 Ala Lys Met Asp Glu Ser Lys Glu Gly Ser Ile Gln Gly Leu Glu Glu 905 910 Met Gln Val Glu Arg Glu Gly Ser Leu Asn Pro Ser Leu Asn Glu Glu 915 920 925 Asn val Lys Gly Gln Gly Glu Lys Lys Glu Glu Ser Glu Glu Glu Asp 930 940

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Lys Glu Glu Glu Glu Glu Glu Lys Leu Glu Glu Glu Lys Glu 945 950 955 Glu Lys Glu Ala Gln Glu Glu Gln Glu Ser Leu Ser Val Gly Glu Glu 965 970 . 975 Glu Asp Lys Glu Glu Gly Leu Glu Glu Ile Tyr Tyr Glu Asp Met Glu 980 985 990 Ser Phe Thr Ile Ser Ser Gly Asn Thr Tyr Phe Val Phe Val Pro Leu 995 1000 1005 Glu Glu Glu His Cys Arg Lys Ser His Ser Thr Phe Ser Ala Met 1010 1020 Phe Ile Asn Asp Thr Ser Ser Ala Lys Phe Ile Glu Gln Val Thr 1025 1030 1035 Ile Pro Ser Arg Leu Ile Leu Glu Ile Lys Lys Gln Leu Phe Ser Glu Gly Gly Asn Phe Ser Pro Lys Glu Ile Asn Ser Leu Cys Ser 1055 1060 1065 Arg Leu Glu Lys Glu Ala Ala Arg Ile Glu Leu Val Glu Ser Val 1070 1080 Ile Met Leu Asn Met Glu Lys Leu Glu Asn Glu Tyr Leu Asp Gln 1085 1090 1095 Ala Asn Asp Val Ile Asn Lys Phe Glu Ser Lys Phe His Asn Leu 1100 1110 1110Ser Val Asp Leu Ile Phe Ile Glu Lys Ile Gln Arg Leu Leu Thr Asn Leu Gln Val Lys Ile Lys Cys Gln Val Ala Lys Ser Asn Ser 1130 1135 1140 Gln Thr Asn Gly Leu Asn Phe Ser Leu Gln Gln Leu Gln Asn Lys 1145 1150 1155 Ile Lys Thr Cys Gln Glu Ser Arg Gly Glu Lys Thr Thr Val Thr 1160 1165 1170 Thr Glu Glu Leu Leu Ser Phe Val Gln Thr Trp Lys Glu Lys Leu 1175 1180 1185 Ser Gln Arg Ile Gln Tyr Leu Asn Cys Ser Leu Asp Arg Val Ser Met Thr Glu Leu Val Phe Thr Asn Thr Ile Leu Lys Asp Gln Glu 1205 1210 1215 Glu Asp Ser Asp Ile Leu Thr Ser Ser Glu Ala Leu Glu Glu Glu 1220 1230 Ala Lys Leu Asp Val Val Thr Pro Glu Ser Phe Thr Gln Leu Ser 1235 1240 1245 Arg Val Gly Lys Pro Leu Ile Glu Asp Pro Ala Val Asp Val Ile

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Arg Lys Leu Leu Gln Leu Pro Asn Thr Lys Trp Pro Thr His His
1265 1270 1275

- Cys Asp Lys Asp Pro Ser Gln Thr Gly Phe Lys Arg His Arg Cys 1280 1285
- Gln Pro Glu Asn Ser Gly Lys Lys Ala Val Pro Ser Ala Ser Ala 1295 1300 1305
- Thr Ser Ala Gly Ser Leu Gln Thr Thr His Pro Pro Leu Ser His 1310 1320
- Ser Phe Thr Pro His Pro Lys Pro Asn Lys Met Glu Arg Lys Tyr
- Arg Val Leu Gly Asp Lys Pro Pro Pro Ala Ala Glu Asp Phe Lys 1340 1350
- Gly Ile leu Thr Leu Leu Trp Glu Ser Ser Glu Asn Leu Leu 1355 1360 1365
- Thr Val Ala Glu Glu Phe Tyr Arg Lys Glu Lys Arg Pro Val Thr
- Arg Pro Asp Cys Met Cys Asp Thr Phe Asp Gln Cys Ala Glu Asn 1385 1390 1395
- Ile Ser Lys Lys Ile Leu Glu Tyr Gln Ser Gln Ala Asn Lys Tyr 1400 1405 1410
- His Asn Ser Cys Leu Ile Glu Leu Arg Ile Gln Ile Arg Arg Phe 1415 1420 1425
- Glu Glu Leu Leu Pro Gln Val Cys Trp Leu Val Met Glu Asn Phe 1430 1440
- Lys Glu His His Trp Lys Lys Phe Phe Thr Ser Val Lys Glu Ile
- Arg Gly Gln Phe Glu Glu Gln Gln Lys Arg Leu Glu Lys Arg Lys 1460 1465 1470
- Asp Lys Asn Ala Gln Lys Leu His Leu Asn Leu Gly His Pro Val 1475 1480 1485
- His Phe Gln Glu Met Glu Ser Leu His Leu Ser Glu Glu Glu Arg 1490 1495 1500
- Gln Glu Glu Leu Asp Ser Met Ile Arg Met Asn Lys Glu Lys Leu 1505 1510 1515
- Glu Glu Cys Thr Arg Arg Asn Gly Gln Val Phe Ile Thr Asn Leu 1520 1530
- Ala Thr Phe Thr Glu Lys Phe Leu Leu Gln Leu Asp Glu Val Val 1535 1540 1545
- Thr Ile Asp Asp Val Gln Val Ala Arg Met Glu Pro Pro Lys Gln 1550 1560
- Lys Leu Ser Met Leu Ile Arg Arg Lys Leu Ala Gly Leu Ser Leu 1565 1570 1575
- Lys Glu Glu Ser Glu Lys Pro Leu Ile Glu Arg Gly Ser Arg Lys 1580 1585 1590

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Trp Pro Gly Ile Lys Pro Thr Glu Val Thr Ile Gln Asn Lys Ile

Leu Leu Gln Pro Thr Ser Ser Ile Ser Thr Thr Lys Thr Thr Leu 1610 1620

Gly His Leu Ala Ala Val Glu Ala Arg Asp Ala Val Tyr Leu Lys 1625 1630 1635

Tyr Leu Ala Ser Phe Glu Glu Glu Leu Lys Arg Ile Gln Asp Asp 1640 1645

Cys Thr Ser Gln Ile Lys Glu Ala Gln Arg Trp Lys Asp Ser Trp 1655 1660 1665

Lys Gln Ser Leu His Thr Ile Gln Gly Leu Tyr Val 1670 1680

<210> 144 <211> 968 <212> PRT <213> Homo sapiens

Met Ala Phe Ala Asn Phe Arg Arg Ile Leu Arg Leu Ser Thr Phe Glu 10 15

Lys Arg Lys Ser Arg Glu Tyr Glu His Val Arg Arg Asp Leu Asp Pro 20 25 30

As Glu Val Trp Glu Ile Val Gly Glu Leu Gly Asp Gly Ala Phe Gly 40 45

Lys Val Tyr Lys Ala Lys Asn Lys Glu Thr Gly Ala Leu Ala Ala Ala 50 55

Lys Val Ile Glu Thr Lys Ser Glu Glu Glu Leu Glu Asp Tyr Ile Val 65 75 80

Glu Ile Glu Ile Leu Ala Thr Cys Asp His Pro Tyr Ile Val Lys Leu $85 \hspace{1.5cm} 90 \hspace{1.5cm} 95$

Leu Gly Ala Tyr Tyr His Asp Gly Lys Leu Trp Ile Met Ile Glu Phe 100 105 110

Cys Pro Gly Gly Ala Val Asp Ala Ile Met Leu Glu Leu Asp Arg Gly 115 120 125

Leu Thr Glu Pro Gln Ile Gln Val Val Cys Arg Gln Met Leu Glu Ala 130 135 140

Leu Asn Phe Leu His Ser Lys Arg Ile Ile His Arg Asp Leu Lys Ala 145 150 155 160

Gly Asn Val Leu Met Thr Leu Glu Gly Asp Ile Arg Leu Ala Asp Phe 165 170 175

Gly Val Ser Ala Lys Asn Leu Lys Thr Leu Gln Lys Arg Asp Ser Phe 180 185 190

Ile Gly Thr Pro Tyr Trp Met Ala Pro Glu Val Val Met Cys Glu Thr

Met Lys Asp Thr Pro Tyr Asp Tyr Lys Ala Asp Ile Trp Ser Leu Gly

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 210 215 220 Ile Thr Leu Ile Glu Met Ala Gln Ile Glu Pro Pro His His Glu Leu 225 230 235 240 Asn Pro Met Arg Val Leu Leu Lys Ile Ala Lys Ser Asp Pro Pro Thr 245 250 255 Leu Leu Thr Pro Ser Lys Trp Ser Val Glu Phe Arg Asp Phe Leu Lys 260 265 270 Ile Ala Leu Asp Lys Asn Pro Glu Thr Arg Pro Ser Ala Ala Gln Leu 275 280 285 Leu Glu His Pro Phe Val Ser Ser Ile Thr Ser Asn Lys Ala Leu Arg Glu Leu Val Ala Glu Ala Lys Ala Glu Val Met Glu Glu Ile Glu Asp 305 310 315 320 Gly Arg Asp Glu Glu Glu Glu Asp Ala Val Asp Ala Ala Ser Thr Leu Glu Asn His Thr Gln Asn Ser Ser Glu Val Ser Pro Pro Ser Leu 340 345 350 Asn Ala Asp Lys Pro Leu Glu Glu Ser Pro Ser Thr Pro Leu Ala Pro 355 360 365 Ser Gln Ser Gln Asp Ser Val Asn Glu Pro Cys Ser Gln Pro Ser Gly 370 375 Asp Arg Ser Leu Gln Thr Thr Ser Pro Pro Val Val Ala Pro Gly Asn 385 390 395 400 Glu Asn Gly Leu Ala Val Pro Val Pro Leu Arg Lys Ser Arg Pro Val 405 410 415 Ser Met Asp Ala Arg Ile Gln Val Ala Gln Glu Lys Gln Val Ala Glu
420 425 430 Gln Gly Gly Asp Leu Ser Pro Ala Ala Asn Arg Ser Gln Lys Ala Ser Gln Ser Arg Pro Asn Ser Ser Ala Leu Glu Thr Leu Gly Gly Glu Lys 450 460 Leu Ala Asn Gly Ser Leu Glu Pro Pro Ala Gln Ala Ala Pro Gly Pro 465 470 475 480 Ser Lys Arg Asp Ser Asp Cys Ser Ser Leu Cys Thr Ser Glu Ser Met 485 490 495 Asp Tyr Gly Thr Asn Leu Ser Thr Asp Leu Ser Leu Asn Lys Glu Met 500 505 510 Gly Ser Leu Ser Ile Lys Asp Pro Lys Leu Tyr Lys Lys Thr Leu Lys 515 520 525 Arg Thr Arg Lys Phe Val Val Asp Gly Val Glu Val Ser Ile Thr Thr $530\,$ Ser Lys Ile Ile Ser Glu Asp Glu Lys Lys Asp Glu Glu Met Arg Phe

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Arg Arg Gln Glu Leu Arg Glu Leu Arg Leu Leu Gln Lys Glu Glu S75 His Arg Asn Gln Thr Gln Leu Ser Asn Lys His Glu Leu Gln Leu Glu 580 585 590 Gln Met His Lys Arg Phe Glu Gln Glu Ile Asn Ala Lys Lys Lys Phe 595 600 605 Phe Asp Thr Glu Leu Glu Asn Leu Glu Arg Gln Gln Lys Gln Gln Val 610 620 Glu Lys Met Glu Gln Asp His Ala Val Arg Arg Arg Glu Glu Ala Arg 625 630 635 Arg Ile Arg Leu Glu Gln Asp Arg Asp Tyr Thr Arg Phe Gln Glu Gln 655 655 Leu Lys Leu Met Lys Lys Glu Val Lys Asn Glu Val Glu Lys Leu Pro 660 670 Arg Gln Gln Arg Lys Glu Ser Met Lys Gln Lys Met Glu Glu His Thr 675 680 685 Gln Lys Lys Gln Leu Leu Asp Arg Asp Phe Val Ala Lys Gln Lys Glu 690 700 Asp Leu Glu Leu Ala Met Lys Arg Leu Thr Thr Asp Asn Arg Arg Glu 705 710 715 720 Ile Cys Asp Lys Glu Arg Glu Cys Leu Met Lys Lys Gln Glu Leu Leu 725 730 735 Arg Asp Arg Glu Ala Ala Leu Trp Glu Met Glu Glu His Gln Leu Gln 740 750 Glu Arg His Gln Leu Val Lys Gln Gln Leu Lys Asp Gln Tyr Phe Leu 755 760 765 Gln Arg His Glu Leu Leu Arg Lys His Glu Lys Glu Arg Glu Gln Met 770 780 Gln Arg Tyr Asn Gln Arg Met Ile Glu Gln Leu Lys Val Arg Gln Gln 785 790 795 800 Gln Glu Lys Ala Arg Leu Pro Lys Ile Gln Arg Ser Glu Gly Lys Thr 805 810 815 Arg Met Ala Met Tyr Lys Lys Ser Leu His Ile Asn Gly Gly Gly Ser 820 830 Ala Ala Glu Gln Arg Glu Lys Ile Lys Gln Phe Ser Gln Glu Glu 835 840 845 Lys Arg Gln Lys Ser Glu Arg Leu Gln Gln Gln Gln Lys His Glu Asn 850 855 860 Gln Met Arg Asp Met Leu Ala Gln Cys Glu Ser Asn Met Ser Glu Leu 865 870 875 880 Gln Gln Leu Gln Asn Glu Lys Cys His Leu Leu Val Glu His Glu Thr 885 890 895 Gln Lys Leu Lys Ala Leu Asp Glu Ser His Asn Gln Asn Leu Lys Glu

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 900 905 910

Trp Arg Asp Lys Leu Arg Pro Arg Lys Lys Ala Leu Glu Glu Asp Leu 915 925

Asn Gln Lys Lys Arg Glu Gln Glu Met Phe Phe Lys Leu Ser Glu Glu 930 935 940

Ala Glu Cys Pro Asn Pro Ser Thr Pro Ser Lys Ala Ala Lys Phe Phe 945 955 960

Pro Tyr Ser Ser Ala Asp Ala Ser

Homo sapiens

Met Ala Leu Gln Leu Ser Arg Glu Gln Gly Ile Thr Leu Arg Gly Ser

Ala Glu Ile Val Ala Glu Phe Phe Ser Phe Gly Ile Asn Ser Ile Leu $20 \hspace{1cm} 25 \hspace{1cm} 30$

Tyr Gln Arg Gly Ile Tyr Pro Ser Glu Thr Phe Thr Arg Val Gln Lys

Tyr Gly Leu Thr Leu Leu Val Thr Thr Asp Leu Glu Leu Ile Lys Tyr

Leu Asn Asn Val Val Glu Gln Leu Lys Asp Trp Leu Tyr Lys Cys Ser

Val Gln Lys Leu Val Val Val Ile Ser Asn Ile Glu Ser Gly Glu Val 85 90 95

Leu Glu Arg Trp Gln Phe Asp Ile Glu Cys Asp Lys Thr Ala Lys Asp 100 105 110

Asp Ser Ala Pro Arg Glu Lys Ser Gln Lys Ala Ile Gln Asp Glu Ile 115 120 125

Arg Ser Val Ile Arg Gln Ile Thr Ala Thr Val Thr Phe Leu Pro Leu 130 140

Leu Glu Val Ser Cys Ser Phe Asp Leu Leu Ile Tyr Thr Asp Lys Asp 145 150 160

Leu Val Val Pro Glu Lys Trp Glu Glu Ser Gly Pro Gln Phe Ile Thr 165 170 175

Asn Ser Glu Glu Val Arg Leu Arg Ser Phe Thr Thr Thr Ile His Lys 180 185 190

Val Asn Ser Met Val Ala Tyr Lys Ile Pro Val Asn Asp 195 200 205

146 591 PRT

Homo sapiens

Met Asn Gly Gln Leu Asp Leu Ser Gly Lys Leu Ile val Lys Ala Gln

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 10 15Tyr Asp Glu Leu Val Leu Met Met Gln Arg Val Phe Arg Gly Lys Leu 35 40 45 Leu Ser Asn Asp Glu Val Thr Ile Lys Tyr Lys Asp Glu Asp Gly Asp 50 55 Leu Ile Thr Ile Phe Asp Ser Ser Asp Leu Ser Phe Ala Ile Gln Cys 65 70 80Ser Arg Ile Leu Lys Leu Thr Leu Phe Val Asn Gly Gln Pro Arg Pro 85 90 95 Leu Glu Ser Ser Gln Val Lys Tyr Leu Arg Arg Glu Leu Ile Glu Leu $100 ext{ } 105 ext{ } .$ Arg Asn Lys Val Asn Arg Leu Leu Asp Ser Leu Glu Pro Pro Gly Glu 115 120 Pro Gly Pro Ser Thr Asn Ile Pro Glu Asn Asp Thr Val Asp Gly Arg 130 135 140 Glu Glu Lys Ser Ala Ser Asp Ser Ser Gly Lys Gln Ser Thr Gln Val 145 150 160 Met Ala Ala Ser Met Ser Ala Phe Asp Pro Leu Lys Asn Gln Asp Glu 165 170 175 Ile Asn Lys Asn Val Met Ser Ala Phe Gly Leu Thr Asp Asp Gln Val Ser Asp Thr Asn Ser Thr Ser Gly Asp Pro Val Glu Lys Lys Asp Glu 195 200 205 Thr Pro Phe Gly Val Ser Val Ala Val Gly Leu Ala Val Phe Ala Cys 210 220 Leu Phe Leu Ser Thr Leu Leu Leu Val Leu Asn Lys Cys Gly Arg Arg 225 230 235 Asn Lys Phe Gly Ile Asn Arg Pro Ala Val Leu Ala Pro Glu Asp Gly Leu Ala Met Ser Leu His Phe Met Thr Leu Gly Gly Ser Ser Leu Ser $260 \hspace{1cm} 265 \hspace{1cm} 270 \hspace{1cm}$ Pro Thr Glu Gly Lys Gly Ser Gly Leu Gln Gly His Ile Ile Glu Asn 275 280 285Pro Gln Tyr Phe Ser Asp Ala Cys Val His His Ile Lys Arg Arg Asp 290 295 300 Ile val Leu Lys Trp Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe 305 310 315 Leu Ala Glu Ser His Asn Leu Leu Pro Glu Gln Asp Lys Met Leu Val Ala val Lys Ala Leu Lys Glu Ala Ser Glu Ser Ala Arg Gln Asp Phe

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln Arg Glu Ala Glu Leu Leu Thr Met Leu Gln His Gln His Ile Val 355 360 365

Arg Phe Phe Gly Val Cys Thr Glu Gly Arg Pro Leu Leu Met Val Phe 370 380 Glu Tyr Met Arg His Gly Asp Leu Asn Arg Phe Leu Arg Ser His Gly 385 390 395 400 Pro Asp Ala Lys Leu Leu Ala Gly Gly Glu Asp Val Ala Pro Gly Pro 405 410 415Leu Gly Leu Gly Gln Leu Leu Ala Val Ala Ser Gln Val Ala Ala Gly 420 425 430 Met Val Tyr Leu Ala Gly Leu His Phe Val His Arg Asp Leu Ala Thr 435 440 445 Arg Asn Cys Leu Val Gly Gln Gly Leu Val Val Lys Ile Gly Asp Phe 450 455 460 Gly Met Ser Arg Asp Ile Tyr Ser Thr Asp Tyr Tyr Arg Val Gly 465 470 475 480Arg Thr Met Leu Pro Ile Arg Trp Met Pro Pro Glu Ser Ile Leu Tyr 485 490 495 Arg Lys Phe Thr Thr Glu Ser Asp Val Trp Ser Phe Gly Val Val Leu 500 510 Trp Glu Ile Phe Thr Tyr Gly Lys Gln Pro Trp Tyr Gln Leu Ser Asn 515 520 525 Thr Glu Ala Ile Asp Cys Ile Thr Gln Gly Arg Glu Leu Glu Arg Pro Arg Ala Cys Pro Pro Glu Val Tyr Ala Ile Met Arg Gly Cys Trp Gln 545 550 555 560 Arg Glu Pro Gln Gln Arg His Ser Ile Lys Asp Val His Ala Arg Leu 565 570 575 Gln Ala Leu Ala Gln Ala Pro Pro Val Tyr Leu Asp Val Leu Gly

<400> 147

Met Gly Glu Ala Glu Lys Phe His Tyr Ile Tyr Ser Cys Asp Leu Asp Ile Asn Val Gln Leu Lys Ile Gly Ser Leu Glu Gly Lys Arg Glu Gln Lys Ser Tyr Asn Ala Val Leu Glu Asp Pro Met Leu Lys Phe Ser Gly 35 40 45Leu Tyr Gln Glu Thr Cys Ser Asp Leu Tyr Val Thr Cys Gln Val Phe Ala Glu Gly Lys Pro Ser Ala Leu Pro Val Arg Thr Ser Tyr Lys Ala

¹⁴⁷ 887

<210> <211> <212> <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Phe Ser Thr Arg Trp Asn Trp Asn Glu Trp Leu Lys Leu Pro Val Lys Tyr Pro Asp Leu Pro Arg Asn Ala Gln Val Ala Leu Thr Ile Trp Asp 100 105 110 Val Tyr Gly Pro Gly Lys Ala Val Pro Val Gly Gly Thr Thr Val Ser 115 120 125 Leu Phe Gly Lys Tyr Gly Met Ser Arg Gln Gly Met His Asp Leu Lys Val Trp Pro Asn Val Glu Ala Asp Gly Ser Glu Pro Thr Asn Thr Pro 145 150 155 160 Gly Arg Thr Ser Ser Thr Leu Ser Glu Asp Gln Met Ser Arg Leu Ala 165 170 175 Lys Leu Thr Lys Ala His Arg Gln Gly His Met Val Lys Val Asp Trp Leu Asp Arg Leu Thr Phe Arg Glu Ile Glu Met Ile Asn Glu Ser Val Lys Arg Ser Ser Asn Phe Met Tyr Leu Met Gly Gly Phe Arg Cys Val Lys Cys Asp Asp Lys Glu Tyr Gly Ile Val Tyr Tyr Glu Lys Asp Gly 225 230 235 240 Asp Glu Ser Ser Pro Ile Leu Thr Ser Phe Glu Leu Val Lys Val Pro Asp Pro Gln Met Ser Leu Glu Asn Leu Val Glu Ser Lys His His Asn 260 265 270 Leu Pro Arg Ser Leu Arg Ser Gly Pro Ser Asp His Asp Leu Lys Pro 275 280 285 Tyr Pro Ser Pro Arg Asp Gln Leu Lys Asn Ile Val Ser Tyr Pro Pro 290 300 Ser Lys Pro Pro Thr Tyr Glu Glu Gln Asp Leu Val Trp Glu Phe Arg Tyr Tyr Leu Thr Asn Gln Asp Lys Ala Leu Thr Lys Ile Leu Thr Ser Val Ile Trp Asp Leu Pro Gln Gly Ala Lys Gln Ala Leu Ala Leu Leu 340 350 Gly Lys Trp Asn Pro Met Asp Val Glu Asp Ser Leu Glu Leu Ile Ser 355 360 . Ser His Tyr Thr Asn Pro Thr Val Arg Arg Tyr Ala Val Ala Arg Leu Arg Gln Ala Asp Asp Glu Asp Leu Leu Met Tyr Leu Ser Gln Leu Val Gln Ala Leu Lys Tyr Glu Asn Phe Asp Asp Ile Lys Asn Gly Leu Glu 405 410 415

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Pro Thr Lys Lys Asp Ser Gln Ser Ser Val Ser Gly Asn Val Ser Asn
420
425
430

Ser Gly Ile Asn Ser Ala Glu Ile Asp Ser Ser Gln Ile Ile Thr Ser 435 440 445 Pro Leu Pro Ser Val Ser Ser Pro Pro Pro Ala Ser Lys Thr Lys Glu 450 455 460 Val Pro Asp Gly Glu Asn Leu Glu Gln Asp Leu Cys Thr Phe Leu Ile 465 470 475 480 Ser Arg Ala Ser Lys Asn Ser Thr Leu Ala Asn Tyr Leu Tyr Trp Tyr
485 490 495 Val Ile Val Glu Cys Glu Asp Gln Asp Thr Gln Gln Arg Asp Pro Lys 500 505 Thr His Glu Met Tyr Leu Asn Val Met Arg Arg Phe Ser Gln Ala Leu 515 520 525 Leu Lys Gly Asp Lys Ser Val Arg Val Met Arg Ser Leu Leu Ala Ala 530 535 540 Gln Gln Thr Phe Val Asp Arg Leu Val His Leu Met Lys Ala Val Gln 545 550 555 560 Arg Glu Ser Gly Asn Arg Lys Lys Lys Asn Glu Arg Leu Gln Ala Leu 565 570 575 Leu Gly Asp Asn Glu Lys Met Asn Leu Ser Asp Val Glu Leu Ile Pro Leu Pro Leu Glu Pro Gln Val Lys Ile Arg Gly Ile Ile Pro Glu Thr Ala Thr Leu Phe Lys Ser Ala Leu Met Pro Ala Gln Leu Phe Phe Lys Thr Glu Asp Gly Gly Lys Tyr Pro Val Ile Phe Lys His Gly Asp Asp 625 630 635 Leu Arg Gln Asp Gln Leu Ile Leu Gln Ile Ile Ser Leu Met Asp Lys Leu Leu Arg Lys Glu Asn Leu Asp Leu Lys Leu Thr Pro Tyr Lys Val Leu Ala Thr Ser Thr Lys His Gly Phe Met Gln Phe Ile Gln Ser Val Pro Val Ala Glu Val Leu Asp Thr Glu Gly Ser Ile Gln Asn Phe Phe Arg Lys Tyr Ala Pro Ser Glu Asn Gly Pro Asn Gly Ile Ser Ala Glu 705 710 715 720 Val Met Asp Thr Tyr Val Lys Ser Cys Ala Gly Tyr Cys Val Ile Thr 725 730 735 Tyr Ile Leu Gly Val Gly Asp Arg His Leu Asp Asn Leu Val Leu Thr Lys Thr Gly Lys Leu Phe His Ile Asp Phe Gly Tyr Ile Leu Gly Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt ASP Pro Lys Pro Leu Pro Pro Pro Met Lys Leu Asn Lys Glu Met Val Glu Gly Met Gly Gly Thr Gln Ser Glu Gln Tyr Gln Glu Phe Arg Lys 785 790 795 800 Gln Cys Tyr Thr Ala Phe Leu His Leu Arg Arg Tyr Ser Asn Leu Ile 805 810 815 Leu Asn Leu Phe Ser Leu Met Val Asp Pro Asn Ile Pro Asp Ile Ala 820 825 Leu Glu Pro Asp Lys Thr Val Lys Lys Val Gln Asp Lys Phe Arg Leu 835 840 Asp Leu Ser Asp Glu Glu Ala Val His Tyr Met Gln Ser Leu Ile Asp 850 860 Glu Ser Val His Ala Leu Phe Ala Ala Val Val Glu Gln Ile His Lys 865 870 875 Phe Ala Gln Tyr Trp Arg Lys

<210> 148 <211> 1290 <212> PRT <213> Homo sapiens

Met Ala Gly Ala Ala Ser Pro Cys Ala Asn Gly Cys Gly Pro Gly Ala 1 10 15

Pro Ser Asp Alá Glu Val Leu His Leu Cys Arg Ser Leu Glu Val Gly 20 30

Thr Val Met Thr Leu Phe Tyr Ser Lys Lys Ser Gln Arg Pro Glu Arg $\frac{35}{45}$

Lys Thr Phe Gln Val Lys Leu Glu Thr Arg Gln Ile Thr Trp Ser Arg $50 \hspace{1.5cm} 60$

Gly Ala Asp Lys Ile Glu Gly Ala Ile Asp Ile Arg Glu Ile Lys Glu 70 70 80

Ile Arg Pro Gly Lys Thr Ser Arg Asp Phe Asp Arg Tyr Gln Glu Asp $90 \\ 90 \\ 95$

Pro Ala Phe Arg Pro Asp Gln Ser His Cys Phe Val Ile Leu Tyr Gly $100 \hspace{1cm} 105 \hspace{1cm} 110$

Met Glu Phe Arg Leu Lys Thr Leu Ser Leu Gln Ala Thr Ser Glu Asp 115 120 125

Glu Val Asn Met Trp Ile Lys Gly Leu Thr Trp Leu Met Glu Asp Thr 130 135 140

Leu Gln Ala Pro Thr Pro Leu Gln Ile Glu Arg Trp Leu Arg Lys Gln 145 150 155 160

Phe Tyr Ser Val Asp Arg Asn Arg Glu Asp Arg Ile Ser Ala Lys Asp 175 175

Leu Lys Asn Met Leu Ser Gln Val Asn Tyr Arg Val Pro Asn Met Arg

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 180 185 190

Phe Leu Arg Glu Arg Leu Thr Asp Leu Glu Gln Arg Ser Gly Asp Ile 195 200 205 Thr Tyr Gly Gln Phe Ala Gln Leu Tyr Arg Ser Leu Met Tyr Ser Ala Gln Lys Thr Met Asp Leu Pro Phe Leu Glu Ala Ser Thr Leu Arg Ala 225 230 235 240 Gly Glu Arg Pro Glu Leu Cys Arg Val Ser Leu Pro Glu Phe Gln Gln 255 255 Phe Leu Leu Asp Tyr Gln Gly Glu Leu Trp Ala Val Asp Arg Leu Gln Val Gln Glu Phe Met Leu Ser Phe Leu Arg Asp Pro Leu Arg Glu Ile 275 280 285 Glu Glu Pro Tyr Phe Phe Leu Asp Glu Phe Val Thr Phe Leu Phe Ser 290 295 300 Lys Glu Asn Ser Val Trp Asn Ser Gln Leu Asp Ala Val Cys Pro Asp 305 310 315 320 Thr Met Asn Asn Pro Leu Ser His Tyr Trp Ile Ser Ser Ser His Asn 325 330 335 Thr Tyr Leu Thr Gly Asp Gln Phe Ser Ser Glu Ser Ser Leu Glu Ala 340 345 Tyr Ala Arg Cys Leu Arg Met Gly Cys Arg Cys Ile Glu Leu Asp Cys 355 360 365 Trp Asp Gly Pro Asp Gly Met Pro Val Ile Tyr His Gly His Thr Leu $370 \hspace{1cm} 375 \hspace{1cm} 380$ Thr Thr Lys Ile Lys Phe Ser Asp Val Leu His Thr Ile Lys Glu His 385 390 395 400 Ala Phe Val Ala Ser Glu Tyr Pro Val Ile Leu Ser Ile Glu Asp His
410 415 Cys Ser Ile Ala Gln Gln Arg Asn Met Ala Gln Tyr Phe Lys Lys Val 420 425 430 Leu Gly Asp Thr Leu Leu Thr Lys Pro Val Glu Ile Ser Ala Asp Gly 435 440 445 Leu Pro Ser Pro Asn Gln Leu Lys Arg Lys Ile Leu Ile Lys His Lys 450 455 460 Lys Leu Ala Glu Gly Ser Ala Tyr Glu Glu Val Pro Thr Ser Met Met 465 470 475 480 Tyr Ser Glu Asn Asp Ile Ser Asn Ser Ile Lys Asn Gly Ile Leu Tyr 485 490 495 Leu Glu Asp Pro Val Asn His Glu Trp Tyr Pro His Tyr Phe Val Leu 500 505 510 Thr Ser Ser Lys Ile Tyr Tyr Ser Glu Glu Thr Ser Ser Asp Gln Gly



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asn Glu Asp Glu Glu Pro Lys Glu Val Ser Ser Thr Glu Leu
530
540

His Ser Asn Glu Lys Trp Phe His Gly Lys Leu Gly Ala Gly Arg Asp 545 550 560 Gly Arg His Ile Ala Glu Arg Leu Leu Thr Glu Tyr Cys Ile Glu Thr 565 570 575 Gly Ala Pro Asp Gly Ser Phe Leu Val Arg Glu Ser Glu Thr Phe Val 580 585 590 Gly Asp Tyr Thr Leu Ser Phe Trp Arg Asn Gly Lys Val Gln His Cys 595 600 605 Arg Ile His Ser Arg Gln Asp Ala Gly Thr Pro Lys Phe Phe Leu Thr 610 620 Asp Asn Leu Val Phe Asp Ser Leu Tyr Asp Leu Ile Thr His Tyr Gln 625 630 635 Gln Val Pro Leu Arg Cys Asn Glu Phe Glu Met Arg Leu Ser Glu Pro 645 650 655 Val Pro Gln Thr Asn Ala His Glu Ser Lys Glu Trp Tyr His Ala Ser Leu Thr Arg Ala Gln Ala Glu His Met Leu Met Arg Val Pro Arg Asp 685 Gly Ala Phe Leu Val Arg Lys Arg Asn Glu Pro Asn Ser Tyr Ala Ile 690 695 700 Ser Phe Arg Ala Glu Gly Lys Ile Lys His Cys Arg Val Gln Gln Glu 705 710 720 Gly Gln Thr Val Met Leu Gly Asn Ser Glu Phe Asp Ser Leu Val Asp 725 730 735 Leu Ile Ser Tyr Tyr Glu Lys His Pro Leu Tyr Arg Lys Met Lys Leu 740 745 750 Arg Tyr Pro Ile Asn Glu Glu Ala Leu Glu Lys Ile Gly Thr Ala Glu 755 760 765 Pro Asp Tyr Gly Ala Leu Tyr Glu Gly Arg Asn Pro Gly Phe Tyr Val Glu Ala Asn Pro Met Pro Thr Phe Lys Cys Ala Val Lys Ala Leu Phe 785 790 795 800 Asp Tyr Lys Ala Gln Arg Glu Asp Glu Leu Thr Phe Ile Lys Ser Ala 805 810 815 Ile Ile Gln Asn Val Glu Lys Gln Glu Gly Gly Trp Trp Arg Gly Asp 820 825 830 Tyr Gly Gly Lys Lys Gln Leu Trp Phe Pro Ser Asn Tyr Val Glu Glu 835 Met Val Asn Pro Val Ala Leu Glu Pro Glu Arg Glu His Leu Asp Glu 850 855 860 Asn Ser Pro Leu Gly Asp Leu Leu Arg Gly Val Leu Asp Val Pro Ala

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 865 870 875 Cys Gln Ile Ala Ile Arg Pro Glu Gly Lys Asn Asn Arg Leu Phe Val Phe Ser Ile Ser Met Ala Ser Val Ala His Trp Ser Leu Asp Val Ala 900 905 910 Ala Asp Ser Gln Glu Glu Leu Gln Asp Trp Val Lys Lys Ile Arg Glu 915 920 925 Val Ala Gln Thr Ala Asp Ala Arg Leu Thr Glu Gly Lys Ile Met Glu 930 940 Arg Arg Lys Lys Ile Ala Leu Glu Leu Ser Glu Leu Val Val Tyr Cys 945 950 955 960 Arg Pro Val Pro Phe Asp Glu Glu Lys Ile Gly Thr Glu Arg Ala Cys 965 970 975 Tyr Arg Asp Met Ser Ser Phe Pro Glu Thr Lys Ala Glu Lys Tyr Val Asn Lys Ala Lys Gly Lys Lys Phe Leu Gln Tyr Asn Arg Leu Gln Leu 995 1000 Ser Arg Ile Tyr Pro Lys Gly Gln Arg Leu Asp Ser Ser Asn Tyr 1010 1020 Asp Pro Leu Pro Met Trp Ile Cys Gly Ser Gln Leu Val Ala Leu 1025 1030 1035 Asn Phe Gln Thr Pro Asp Lys Pro Met Gln Met Asn Gln Ala Leu 1040 1050 Phe Met Thr Gly Arg His Cys Gly Tyr Val Leu Gln Pro Ser Thr 1055 1060 1065 Met Arg Asp Glu Ala Phe Asp Pro Phe Asp Lys Ser Ser Leu Arg 1070 1080 Gly Leu Glu Pro Cys Ala Ile Ser Ile Glu Val Leu Gly Ala Arg 1085 1090 1095 His Leu Pro Lys Asn Gly Arg Gly Ile Val Cys Pro Phe Val Glu Ile Glu Val Ala Gly Ala Glu Tyr Asp Ser Thr Lys Gln Lys Thr 1115 1120 1125 Glu Phe Val Val Asp Asn Gly Leu Asn Pro Val Trp Pro Ala Lys 1130 1140 Pro Phe His Phe Gln Ile Ser Asn Pro Glu Phe Ala Phe Leu Arg Phe Val Val Tyr Glu Glu Asp Met Phe Ser Asp Gln Asn Phe Leu Ala Gln Ala Thr Phe Pro Val Lys Gly Leu Lys Thr Gly Tyr Arg 1175 1180 1185 Ala Val Pro Leu Lys Asn Asn Tyr Ser Glu Asp Leu Glu Leu Ala

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ser Leu Leu Ile Lys Ile Asp Ile Phe Pro Ala Lys Glu Asn Gly
1205 1210 1215

Asp Leu Ser Pro Phe Ser Gly Thr Ser Leu Arg Glu Arg Gly Ser 1220 1225 1230

Asp Ala Ser Gly Gln Leu Phe His Gly Arg Ala Arg Glu Gly Ser 1235 1240 1245

Phe Glu Ser Arg Tyr Gln Gln Pro Phe Glu Asp Phe Arg Ile Ser 1250 1260

Gln Glu His Leu Ala Asp His Phe Asp Ser Arg Glu Arg Arg Ala 1265 1270 1275

Pro Arg Arg Thr Arg Val Asn Gly Asp Asn Arg Leu 1280 1285 1290

<210> 149

<211> 200

<213> Homo sapiens

<400> 149

Met Val Ser Ile Ser Leu Lys Phe Tyr Lys Glu Leu Gln Ala His Gly 1 10 15

Ala Asp Glu Leu Leu Lys Arg Val Tyr Gly Ser Phe Leu Val Asn Pro 20 30

Glu Ser Gly Tyr Asn Val Ser Leu Leu Tyr Asp Leu Glu Asn Leu Pro 35 45

Ala Ser Lys Asp Ser Ile Val His Gln Ala Gly Met Leu Lys Arg Asn $50 \hspace{0.5in} 60$

Cys Phe Ala Ser Val Phe Glu Lys Tyr Phe Gln Phe Gln Glu Glu Gly 70 75 80

Lys Glu Gly Glu Asn Arg Ala Val Ile His Tyr Arg Asp Asp Glu Thr $85 \hspace{1cm} 90 \hspace{1cm} 95$

Met Tyr Val Glu Ser Lys Lys Asp Arg Val Thr Val Val Phe Ser Thr 100 105 110

Val Phe Lys Asp Asp Asp Asp Val Val Ile Gly Lys Val Phe Met Gln 115 120 125

Glu Phe Lys Glu Gly Arg Arg Ala Ser His Thr Ala Pro Gln Val Leu 130 140

Phe Ser His Arg Glu Pro Pro Leu Glu Leu Lys Asp Thr Asp Ala Ala 145 150 155 160

Val Gly Asp Asn Ile Gly Tyr Ile Thr Phe Cys Ala Val Pro Phe Val 165 170 175

His Gln Cys Gln Cys Ser Arg His Thr Ile Asn Leu Val Pro His Val

Pro Gly Leu Pro Pro Leu Pro His

<210> 150

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

<400> 150

Met Ala Arg Leu Arg Ala Gly Ile Tyr Leu Ala Ser Gl $\mathfrak n$ Phe Phe Gly 10 15

Trp Lys Glu Gln Glu Ile Ser Ser Tyr Ser Pro Val Glu Arg Ser Gly

Leu Ser Leu Gly

<210> 151 <211> 593 <212> PRT <213> Homo sapiens

Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala 1 10 15

Glu Asn Leu Leu Thr Arg Gly Val Asp Gly Ser Phe Leu Ala Arg

Pro Ser Lys Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn

Gly Ala Val Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp 50 60

Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr 65 70 75 80

Tyr Met Glu His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile 85 90 95

Glu Leu Lys Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp 100 105 110

Phe His Gly His Leu Ser Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu 115 120 125

Lys Gly Lys His Gly Ser Phe Leu Val Arg Glu Ser Gln Ser His Pro 130 140

Gly Asp Phe Val Leu Ser Val Arg Thr Gly Asp Asp Lys Gly Glu Ser 145 150 155

Asn Asp Gly Lys Ser Lys Val Thr His Val Met Ile Arg Cys Gln Glu 165 170 175

Leu Lys Tyr Asp val Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp 180 185

Leu Val Glu His Tyr Lys Lys Asn Pro Met Val Glu Thr Leu Gly Thr $195 \hspace{0.2in} 200 \hspace{0.2in} 205$

Val Leu Gln Leu Lys Gln Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala 210 215 220

Glu Ile Glu Ser Arg Val Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr 225 230 235

Asp Lys Val Lys Gln Gly Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln 255

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln Glu Cys Lys Leu Leu Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu 265 270 Asn Lys Asn Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr 275 280 285 Arg Val Val Leu His Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr Ile Asn Ala Asn Ile Ile Met Pro Glu Phe Glu Thr Lys Cys Asn Asn 305 310 315 Ser Lys Pro Lys Lys Ser Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn 325 330 335Thr Val Asn Asp Phe Trp Arg Met Val Phe Gln Glu Asn Ser Arg Val 340 345Ile Val Met Thr Thr Lys Glu Val Glu Arg Gly Lys Ser Lys Cys Val 355 360 365 Lys Tyr Trp Pro Asp Glu Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg Val Arg Asn Val Lys Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu 385 390 395 400 Leu Lys Leu Ser Lys Val Gly Gln Gly Asn Thr Glu Arg Thr Val Trp 405 410 415 Gln Tyr His Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro 420 425 430 Gly Gly Val Leu Asp Phe Leu Glu Glu Val His His Lys Gln Glu Ser 435 440 445 Ile Met Asp Ala Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly 450 460 Arg Thr Gly Thr Phe Ile Val Ile Asp Ile Leu Ile Asp Ile Ile Arg 465 470 475 480Glu Lys Gly Val Asp Cys Asp Ile Asp Val Pro Lys Thr Ile Gln Met 485 490 495 Val Arg Ser Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Arg Phe Ile Tyr Met Ala Val Gln His Tyr Ile Glu Thr Leu Gln Arg Arg 515 520 525 Ile Glu Glu Glu Gln Lys Ser Lys Arg Lys Gly His Glu Tyr Thr Asn 530 540 Ile Lys Tyr Ser Leu Ala Asp Gln Thr Ser Gly Asp Gln Ser Pro Leu 545 550 560 Pro Pro Cys Thr Pro Thr Pro Pro Cys Ala Glu Met Arg Glu Asp Ser 575 Ala Arg Val Tyr Glu Asn Val Gly Leu Met Gln Gln Gln Lys Ser Phe 580 585 590

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

152 348 PRT Homo sapiens <400> 152 Met Ala Gly Ser Leu Pro Pro Cys Val Val Asp Cys Gly Thr Gly Tyr Thr Lys Leu Gly Tyr Ala Gly Asn Thr Glu Pro Gln Phe Ile Ile Pro Ser Cys Ile Ala Ile Arg Glu Ser Ala Lys Val Val Asp Gln Ala Gln $\frac{35}{40}$ Arg Arg Val Leu Arg Gly Val Asp Asp Leu Asp Phe Phe Ile Gly Asp Glu Ala Ile Asp Lys Pro Thr Tyr Ala Thr Lys Trp Pro Ile Arg His Gly Ile Ile Glu Asp Trp Asp Leu Met Glu Arg Phe Met Glu Gln Val Val Phe Lys Tyr Leu Arg Ala Glu Pro Glu Asp His Tyr Phe Leu Met 100 105 110 Thr Glu pro Pro Leu Asn Thr Pro Glu Asn Arg Glu Tyr Leu Ala Glu 115 120 125 Ile Met Phe Glu Ser Phe Asn Val Pro Gly Leu Tyr Ile Ala Val Gln
130 140 Ala Val Leu Ala Leu Ala Ala Ser Trp Thr Ser Arg Gln Val Gly Glu
145 150 155 160 Arg Thr Leu Thr Gly Ile Val Ile Asp Ser Gly Asp Gly Val Thr His 165 170 175 Val Ile Pro Val Ala Glu Gly Tyr Val Ile Gly Ser Cys Ile Lys His 180 185 Ile Pro Ile Ala Gly Arg Asp Ile Thr Tyr Phe Ile Gln Gln Leu Leu 195 200 205Arg Glu Arg Glu Val Gly Ile Pro Pro Glu Gln Ser Leu Glu Thr Ala 210 225 220 Lys Ala Ile Lys Glu Lys Tyr Cys Tyr Ile Cys Pro Asp Ile Val Lys 225 230 235 240 Glu Phe Ala Lys Tyr Asp Val Asp Pro Arg Lys Trp Ile Lys Gln Tyr 245 250 255

Thr Gly Ile Asn Ala Ile Asn Gln Lys Lys Phe Val Ile Asp Val Gly

Tyr Glu Arg Phe Leu Gly Pro Glu Ile Phe Phe His Pro Glu Phe Ala 275 280 285

Asn Pro Asp Phe Met Glu Ser Ile Ser Asp Val Val Asp Glu Val Ile

322/403

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln Asn Cys Pro Ile Asp Val Arg Arg Pro Leu Tyr Lys Pro Glu Phe 305 310 315 320

Phe Gln Val Cys His Thr Lys Lys Asp Tyr Glu Glu Tyr Gly Pro Ser 325 330 335

Ile Cys Arg His Asn Pro Val Phe Gly Val Met Ser

<210> <211> <212> <213>

153 248 PRT Homo sapiens

<400> 153

Met Phe Leu Ala Lys Ala Leu Leu Glu Gly Ala Asp Arg Gly Leu Gly

Glu Ala Leu Gly Gly Leu Phe Gly Gly Gly Gly Gln Arg Glu Gly 20 25 30

Gly Gly Arg Asn Ile Gly Gly Ile Val Gly Gly Ile Val Asn Phe Ile

Ser Glu Ala Ala Ala Ala Gln Tyr Thr Pro Glu Pro Pro Pro Thr Gln 50 60

Gln His Phe Thr Ser Val Glu Ala Ser Glu Ser Glu Glu Val Arg Arg 65 70 75 80

Phe Arg Gln Gln Phe Thr Gln Leu Ala Gly Pro Asp Met Glu Val Gly 90 95

Ala Thr Asp Leu Met Asn Ile Leu Asn Lys Val Leu Ser Lys His Lys $100 \ 105 \ 110$

Asp Leu Lys Thr Asp Gly Phe Ser Leu Asp Thr Cys Arg Ser Ile Val 115 120 125

Ser Val Met Asp Ser Asp Thr Thr Gly Lys Leu Gly Phe Glu Glu Phe 130 140

Lys Tyr Leu Trp Asn Asn Ile Lys Lys Trp Gln Cys Val Tyr Lys Gln 145 150 150 160

Tyr Asp Arg Asp His Ser Gly Ser Leu Gly Ser Ser Gln Leu Arg Gly 175

Ala Leu Gln Ala Ala Gly Phe Gln Leu Asn Glu Gln Leu Tyr Gln Met 180 185 190

Ile Val Arg Arg Tyr Ala Asn Glu Asp Gly Asp Met Asp Phe Asn Asn 195 200

Phe Ile Ser Cys Leu Val Arg Leu Asp Ala Met Phe Arg Ala Phe Lys 210 220

Ser Leu Asp Arg Asp Arg Asp Gly Leu Ile Gln Val Ser Ile Lys Glu 225 230 235 240

Trp Leu Gln Leu Thr Met Tyr Ser 245

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <212> PRT <213> Homo sapiens

<400> 154 Met Ala Leu Gln Leu Glu Val Val His Gly Pro Asp Ile Ile Thr Glu 1 10 15 Thr Asp Val Val Thr Glu Gly Val Ile Val Pro Glu Ala Val Leu Glu Ala Asp Val Ala Ile Glu Glu Asp Leu Glu Glu Asp Asp Gly Asp His 35 40 45Ile Leu Thr Ser Glu Leu Ile Thr Glu Thr Val Arg Val Pro Glu Gln Val Phe Val Ala Asp Leu Val Thr Gly Pro Asn Gly His Leu Glu His 65 70 75 80 Val Val Gln Asp Cys Val Ser Gly Val Asp Ser Pro Thr Met Val Ser Glu Glu Val Leu Val Thr Asn Ser Asp Thr Glu Thr Val Ile Gln Ala Ala Gly Gly Val Pro Gly Ser Thr Val Thr Ile Lys Thr Glu Asp Asp Asp Asp Asp Val Lys Ser Thr Ser Glu Asp Tyr Leu Met Ile Ser Leu Asp Asp Val Gly Glu Lys Leu Glu His Met Gly Asn Thr Pro Leu 145 150 150 155Lys Ile Gly Ser Asp Gly Ser Gln Glu Asp Ala Lys Glu Asp Gly Phe Gly Ser Glu Val Ile Lys Val Tyr Ile Phe Lys Ala Glu Ala Glu Asp 180 185 190 Asp Val Glu Ile Gly Gly Thr Glu Met Ser Pro Glu Ser Glu Tyr Thr 195 200 205Ser Gly His Ser Val Ala Gly Val Leu Asp Gln Ser Arg Met Gln Arg Glu Lys Met Val Tyr Met Ala Val Lys Asp Ser Ser Gln Glu Glu Asp 225 230 235 240 Asp Ile Arg Asp Glu Arg Arg Val Ser Arg Arg Tyr Glu Asp Cys Gln 255 Ala Ser Gly Asn Thr Leu Asp Ser Ala Leu Glu Ser Arg Ser Ser Thr Ala Ala Gln Tyr Leu Gln Ile Cys Asp Gly Ile Asn Thr Asn Lys Val 275 280 285 Leu Lys Gln Lys Ala Lys Lys Arg Arg Gly Glu Thr Arg Gln Trp Gln Thr Ala Val Ile Ile Gly Pro Asp Gly Gln Pro Leu Thr Val Tyr 305 310 315 320 Pro Cys His Ile Cys Thr Lys Lys Phe Lys Ser Lys Gly Phe Leu Lys



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 325 330 335 Arg His Met Lys Asn His Pro Asp His Leu Met Arg Lys Lys Tyr Gln 340 345 Cys Thr Asp Cys Asp Phe Thr Thr Asn Lys Lys Val Ser Phe His Asn 355 360 His Leu Glu Ser His Lys Leu Ile Asn Lys Val Asp Lys Thr His Glu 370 375 380 Phe Thr Glu Tyr Thr Arg Arg Tyr Arg Glu Ala Ser Pro Leu Ser Ser 385 390 395 400 Asn Lys Leu Ile Leu Arg Asp Lys Glu Pro Lys Thr Asp Lys Cys Lys 405 410 415 Tyr Cys Asp Tyr Glu Thr Ala Glu Gln Gly Leu Leu Asn Arg His Leu
420 425 430 Leu Ala Val His Ser Lys Asn Phe Pro His Val Cys Val Glu Cys Gly
435 440 445 Lys Gly Phe Arg His Pro Ser Glu Leu Lys Lys His Met Arg Thr His 450 460 Thr Gly Glu Lys Pro Tyr Gln Cys Gln Tyr Cys Ile Phe Arg Cys Ala Asp Gln Ser Asn Leu Lys Thr His Ile Lys Ser Lys His Gly Asn Asn 485 490 495 Leu Pro Tyr Lys Cys Glu His Cys Pro Gln Ala Phe Gly Asp Glu Arg Glu Leu Gln Arg His Leu Asp Leu Phe Gln Gly His Lys Thr His Gln 515 520 525 Cys Pro His Cys Asp His Lys Ser Thr Asn Ser Ser Asp Leu Lys Arg His Ile Ile Ser Val His Thr Lys Asp Phe Pro His Lys Cys Glu Val 545 550 560 Cys Asp Lys Gly Phe His Arg Pro Ser Glu Leu Lys Lys His Ser Asp 565 570 575 Ile His Lys Gly Arg Lys Ile His Thr Cys Arg His Cys Asp Phe Lys 580 585 590 Thr Ser Asp Pro Phe Ile Leu Ser Gly His Leu Leu Ser Val His Thr 595 600 605 Lys Asp Gln Pro Leu Lys Cys Lys Gly Cys Thr Arg Gly Phe Arg Gln 610 615 Gln Asn Glu Leu Lys Lys His Met Lys Thr His Thr Gly Arg Lys Ser 625 630 635 640 Tyr Gln Cys Glu Tyr Cys Glu Tyr Ser Thr Thr Asp Ala Ser Gly Phe $645 \hspace{0.5cm} 650 \hspace{0.5cm} 655$ Lys Arg His Val Ile Ser Ile His Thr Lys Asp Tyr Pro His Arg Cys 660 665 670



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Phe Cys Asn Lys Gly Phe Arg Arg Pro Ser Glu Lys Asn Gln His
675
685

Ile Met Lys His His Lys Glu Ala Leu Met 690 695

<210> 155

<211> 77

<213> Homo sapiens

<400> 155

Met Ile Met Gln Asp Phe Val Ala Gly Met Ala Gly Thr Ala His Ile $10 \ 15$

Asp Gly Asp His Ile Val Val Ser Val Pro Glu Ala Val Leu Val Ser

Asp val val Thr Asp Asp Gly Ile Thr Leu Asp His Gly Leu Ala Ala 35 40

Glu Val Val His Gly Pro Asp Ile Ile Thr Glu Thr Asp Val Val Thr $50 \hspace{1.5cm} 60$

Glu Gly Val Ile Val Pro Glu Ala Val Leu Glu Ala Asp Val Ala Ile 65 70 75 80

Glu Glu Asp Leu Glu Glu Asp Asp Gly Asp His Ile Leu Thr Ser Glu 85 90 95

Leu Ile Thr Glu Thr Val Arg Val Pro Glu Gln Val Phe Val Ala Asp 100 105 110

Leu Val Thr Gly Pro Asn Gly His Leu Glu His Val Val Gln Asp Cys 115 120 125

val Ser Gly Val Asp Ser Pro Thr Met Val Ser Glu Glu Val Leu Val 130 135 140

Thr Asn Ser Asp Thr Glu Thr Val Ile Gln Ala Ala Gly Gly Val Pro 145 150 155 160

Gly Ser Thr Val Thr Ile Lys Thr Glu Asp Asp Asp Asp Asp Asp Val

Lys Ser Thr Ser Glu Asp Tyr Leu Met Ile Ser Leu Asp Asp Val Gly 180 185 190

Glu Lys Leu Glu His Met Gly Asn Thr Pro Leu Lys Ile Gly Ser Asp 195 200 205

Gly Ser Gln Glu Asp Ala Lys Glu Asp Gly Phe Gly Ser Glu Val Ile 210 220

Lys Val Tyr Ile Phe Lys Ala Glu Ala Glu Asp Asp Val Glu Ile Gly 225 230 235 240

Gly Thr Glu Ile Val Thr Glu Ser Glu Tyr Thr Ser Gly His Ser Val 245 250 255

Ala Gly Val Leu Asp Gln Ser Arg Met Gln Arg Glu Lys Met Val Tyr 260 265 270

Met Ala Val Lys Asp Ser Ser Gln Glu Glu Asp Asp Ile Ser Cys Ala 275 280 285 Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Ile Ala Asp Glu Val Tyr Met Glu Val Ile Val Gly Glu Glu Glu 290 300 Gly Thr Ser Leu Pro Glu Ile Gln Leu Glu Asp Ser Asp Val Asn Lys 305 310 315 Thr Val Val Pro Val Val Trp Ala Ala Tyr Gly Asn Thr Leu Asp 325 330 335 Ser Ala Leu Glu Ser Arg Ser Ser Thr Ala Ala Gln Tyr Leu Gln Ile 340 345 350 Cys Asp Gly Ile Asn Thr Asn Lys Val Leu Lys Gln Lys Ala Lys Lys Arg Arg Gly Glu Thr Arg Gln Trp Gln Thr Ala Val Ile Ile Gly 370 380 Pro Asp Gly Gln Pro Leu Thr Val Tyr Pro Cys His Ile Cys Thr Lys Lys Phe Lys Ser Arg Gly Phe Leu Lys Arg His Met Lys Asn His Pro Asp His Leu Met Arg Lys Lys Tyr Gln Cys Thr Asp Cys Asp Phe Thr $420 \ \ 425 \ \ 430$ Thr Asn Lys Lys Val Ser Phe His Asn His Leu Glu Ser His Lys Leu 435 445 ` Ile Asn Lys Val Asp Lys Thr His Glu Phe Thr Glu Tyr Thr Arg Arg 450 455 460 Tyr Arg Glu Ala Ser Pro Leu Ser Ser Asn Lys Leu Ile Leu Arg Asp
465 470 475 480 Lys Glu Pro Lys Met His Lys Cys Lys Tyr Cys Asp Tyr Glu Thr Ala 485 490 495 Glu Gln Gly Leu Leu Asn Arg His Leu Leu Ala Val His Ser Lys Asn 500 505 510 Phe Pro His Val Cys Val Glu Cys Gly Lys Gly Phe Arg His Pro Ser 515 525 Glu Leu Lys Lys His Met Arg Thr His Thr Gly Glu Lys Pro Tyr Gln Cys Gln Tyr Cys Ile Phe Arg Cys Ala Asp Gln Ser Asn Leu Lys Thr 545 550 555 560 His Ile Lys Ser Lys His Gly Asn Asn Leu Pro Tyr Lys Cys Glu His 565 570 575 Cys Pro Gln Ala Phe Gly Asp Glu Arg Glu Leu Gln Arg His Leu Asp 580 585 Leu Phe Gln Gly His Lys Thr His Gln Cys Pro His Cys Asp His Lys Ser Thr Asn Ser Ser Asp Leu Lys Arg His Ile Ile Ser Val His Thr 610 620

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Lys Asp Phe Pro His Lys Cys Glu Val Cys Asp Lys Gly Phe His Arg
625 630 635 640

Pro Ser Glu Leu Lys Lys His Ser Asp Ile His Lys Gly Arg Lys Ile 645 650 His Gln Cys Arg His Cys Asp Phe Lys Thr Ser Asp Pro Phe Ile Leu Ser Gly His Ile Leu Ser Val His Thr Lys Asp Gln Pro Leu Lys Cys 675 680 685 Lys Arg Cys Lys Arg Gly Phe Arg Gln Gln Asn Glu Leu Lys Lys His Met Lys Thr His Thr Gly Arg Lys Ile Tyr Gln Cys Glu Tyr Cys Glu 705 710 715 720 Tyr Ser Thr Thr Asp Ala Ser Gly Phe Lys Arg His Val Ile Ser Ile His Thr Lys Asp Tyr Pro His Arg Cys Glu Phe Cys Lys Lys Gly Phe Arg Arg Pro Ser Glu Lys Asn Gln His Ile Met Arg His His Lys Glu

Ala Leu Met 770

<210> 156 <211> 1390 <212> PRT <213> Homo sapiens

<400> 156

Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 60 Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp 100 105 110 Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp 115 120 125 Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His 130 140 Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys 145 150 155 160

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val 165 170 175 Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe 180 185 190 Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp 210 215 220 Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu 225 230 240 Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn 245 250 250 Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln 260 265 270 Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg 290 295 300 Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala 305 310 315 320 Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser 325 330 335Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys 355 360 365Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg 370 375 380 Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr 405 410 415 Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly 420 430 Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445$ Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln 450 455 460 Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu 465 470 475 480 Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu 485 490 495 Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 500 505 510

The Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln 515 520 525 Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile 545 550 555 560 Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu 565 570 575 Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg 585 590 Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys 610 620 Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile 625 630 635 Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp 645 655 Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly 660 665 670 Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg 675 680 His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe 705 710 715 720 Ala val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn 755 760 765 Ser val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg 770 780 Asn phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys 805 810 815 Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp 820 830 Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val 835 840

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp

850

850

Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys 865 870 875

Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val 885 890 895

Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys 900 905 910

Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp 915 920 925

Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala 930 940

Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln $945 \hspace{0.5cm} 950 \hspace{0.5cm} 955 \hspace{0.5cm} 960$

Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His $965 \hspace{1cm} 970 \hspace{1cm} 975$

Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr 980 985

Thr Glu Met Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro 995 1000 1005

Glu Asp Gln Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln 1010 1020

Val Gln Tyr Pro Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly 1035 1036

Asp Ser Asp Ile Ser Ser Pro Leu Leu Gln Asn Thr Val His Ile 1040 1050

Asp Leu Ser Ala Leu Asn Pro Glu Leu Val Gln Ala Val Gln His 1055 1066

Val Val. Ile Gly Pro Ser Ser Leu Ile Val His Phe Asn Glu Val 1070 1080

Ile Gly Arg Gly His Phe Gly Cys Val Tyr His Gly Thr Leu Leu 1085 1090 1095

Asp Asn Asp Gly Lys Lys Ile His Cys Ala Val Lys Ser Leu Asn 1100 1110

Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe Leu Thr Glu Gly 1115 1120 1125

Ile Ile Met Lys Asp Phe Ser His Pro Asn Val Leu Ser Leu Leu 1130 1140

Gly Ile Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val Leu Pro 1145 1150 1155

Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu Thr

His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 1175 1180 1185

Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg 1190 1195 1200

Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe Thr Val 1205 1215

Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu 1220 1230

Tyr Tyr Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys 1235 1240 1245

Trp Met Ala Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys

Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Leu Met Thr

Arg Gly Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr 1280 1285 1290

Val Tyr Leu Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu Tyr Cys 1295 1300 1305

Pro Asp Pro Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys 1310 1320

Ala Glu Met Arg Pro Ser Phe Ser Glu Leu Val Ser Arg Ile Ser 1330 1335

Ala Ile Phe Ser Thr Phe Ile Gly Glu His Tyr Val His Val Asn 1340 1345 1350

Ala Thr Tyr Val Asn Val Lys Cys Val Ala Pro Tyr Pro Ser Leu 1355 1360 1365

Leu Ser Ser Glu Asp Asn Ala Asp Asp Glu Val Asp Thr Arg Pro

Ala Ser Phe Trp Glu Thr Ser 1385 1390

<210> 157 <211> 213 <212> PRT <213> Homo

<400> 157

Met Thr Asp Ala Thr Val Ser Phe Ala Lys Asp Phe Leu Ala Gly Gly 1 10 15

Val Ala Ala Ala Ile Ser Lys Met Ala Val Val Pro Ile Gln Arg Val

Lys Leu Leu Gln Val Gln His Ala Ser Lys Gln Val Thr Ala Asp 35 40 45

Lys Gln Tyr Lys Gly Ile Ile Asp Cys Val Val Cys Ile Ser Lys Glu

Gln Gly Val Leu Ser Phe Trp Arg Gly Asn Leu Ala Asn Val Ile Arg 65 70 75 80

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Tyr Phe Pro Thr Gln Ala Phe Asn Phe Ala Phe Lys Asp Lys Tyr Lys
85 90 95

Gln Ile Phe Leu Gly Asp Val Asp Lys Arg Thr Gln Phe Trp Arg Tyr 100 105 110 Phe Glu Gly Asn Leu Thr Ser Gly Ser Ala Ala Gly Ala Thr Ser Leu Cys Phe Val Tyr Pro Leu Asp Phe Ala Leu Thr Arg Leu Ala Ala Asn Val Gly Lys Ala Gly Ala Glu Arg Glu Phe Arg Ser Leu Gly Asp Cys 145 155 160 Leu Val Lys Ile Tyr Lys Ser Asp Gly Ile Lys Gly Leu Tyr Gln Gly 175 175Phe Asn Met Ser Val Gln Gly Ile Ile Tyr Arg Ala Ala Tyr Phe 180 185 190 Ser Ile Tyr Asp Thr Ala Lys Gly Met Leu Pro Asp Pro Lys Asn Thr 195 200 205 His Ile Leu Ile Ser 210

158 608 PRT

Homo sapiens

Ser Gly Trp Glu Ser Tyr Tyr Lys Thr Glu Gly Asp Glu Glu Ala Glu 1 10 15 Glu Glu Glu Glu Asn Leu Glu Ala Ser Gly Asp Tyr Lys Tyr Ser 20 25 30 Gly Arg Asp Ser Leu Ile Phe Leu Val Asp Ala Ser Lys Ala Met Phe Glu Ser Gln Ser Glu Asp Glu Leu Thr Pro Phe Asp Met Ser Ile Gln 50 60 Cys Ile Gln Ser Val Tyr Ile Ser Lys Ile Ile Ser Ser Asp Arg Asp 65 70 75 80Leu Leu Ala Val Val Phe Tyr Gly Thr Glu Lys Asp Lys Asn Ser Val 85 90 95 Asn Phe Lys Asn Ile Tyr Val Leu Gln Glu Leu Asp Asn Pro Gly Ala 100 105 110 Lys Arg Ile Leu Glu Leu Asp Gln Phe Lys Gly Gln Gln Gly Gln Lys Arg Phe Gln Asp Met Met Gly His Gly Ser Asp Tyr Ser Leu Ser Glu 130 135 140 Val Leu Trp Val Cys Ala Asn Leu Phe Ser Asp Val Gln Phe Lys Met 145 150 160 Ser His Lys Arg Ile Met Leu Phe Thr Asn Glu Asp Asn Pro His Gly 165 170 175

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asn Asp Ser Ala Lys Ala Ser Arg Ala Arg Thr Lys Ala Gly Asp Leu
180
185
190

Arg Asp Thr Gly Ile Phe Leu Asp Leu Met His Leu Lys Lys Pro Gly 195 200 205Gly Phe Asp Ile Ser Leu Phe Tyr Arg Asp Ile Ile Ser Ile Ala Glu 210 215 220 Asp Glu Asp Leu Arg Val His Phe Glu Glu Ser Ser Lys Leu Glu Asp 230 235 240 Leu Leu Arg Lys Val Arg Ala Lys Glu Thr Arg Lys Arg Ala Leu Ser Arg Leu Lys Leu Lys Leu Asn Lys Asp Ile Val Ile Ser Val Gly Ile $260 \hspace{0.25cm} 265 \hspace{0.25cm} 270 \hspace{0.25cm}$ Tyr Asn Leu Val Gln Lys Ala Leu Lys Pro Pro Pro Ile Lys Leu Tyr 275 280 285 Arg Glu Thr Asn Glu Pro Val Lys Thr Lys Thr Arg Thr Phe Asn Thr 290 295 300Ser Thr Gly Gly Leu Leu Leu Pro Ser Asp Thr Lys Arg Ser Gln Ile 305 310 315 320 Tyr Gly Ser Arg Gln Ile Ile Leu Glu Lys Glu Glu Thr Glu Glu Leu Lys Arg Phe Asp Asp Pro Gly Leu Met Leu Met Gly Phe Lys Pro Leu 340 345 Pro Leu 350Val Leu Leu Lys Lys His His Tyr Leu Arg Pro Ser Leu Phe Val Tyr 355 360 365 Pro Glu Glu Ser Leu Val Ile Gly Ser Ser Thr Leu Phe Ser Ala Leu Leu Ile Lys Cys Leu Glu Lys Glu Val Ala Ala Leu Cys Arg Tyr Thr 385 390 395 400 Pro Arg Arg Asn Ile Pro Pro Tyr Phe Val Ala Leu Val Pro Gln Glu 405 410 415Glu Glu Leu Asp Asp Gln Lys Ile Gln Val Thr Pro Pro Gly Phe Gln
420 425 430 Leu Val Phe Leu Pro Phe Ala Asp Asp Lys Arg Lys Met Pro Phe Thr Glu Lys Ile Met Ala Thr Pro Glu Gln Val Gly Lys Met Lys Ala Ile 450 455 460 Val Glu Lys Leu Arg Phe Thr Tyr Arg Ser Asp Ser Phe Glu Asn Pro 465 470 480 Val Leu Gln Gln His Phe Arg Asn Leu Glu Ala Leu Ala Leu Asp Leu
485
490
495 Met Glu Pro Glu Gln Ala Val Asp Leu Thr Leu Pro Lys Val Glu Ala Met Asn Lys Arg Leu Gly Ser Leu Val Asp Glu Phe Lys Glu Leu Val WO 2004/009622 PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Tyr Pro Pro Asp Tyr Asn Pro Glu Gly Lys Val Thr Lys Arg Lys His 530 535

Asp Asn Glu Gly Ser Gly Ser Lys Arg Pro Lys Val Glu Tyr Ser Glu 545 550 560

Glu Glu Leu Lys Thr His Ile Ser Lys Gly Thr Leu Gly Lys Phe Thr 565 570 575

Val Pro Met Leu Lys Glu Ala Cys Arg Ala Tyr Gly Leu Lys Ser Gly 580 585

Leu Lys Lys Gln Glu Leu Leu Glu Ala Leu Thr Lys His Phe Gln Asp

159 168 PRT

<210> <211> <212> <213>

Homo sapiens

Met Phe Gln Ile Pro Glu Phe Glu Pro Ser Glu Gln Glu Asp Ser Ser 1 10 15

Ser Ala Glu Arg Gly Leu Gly Pro Ser Pro Ala Gly Asp Gly Pro Ser

Gly Ser Gly Lys His His Arg Gln Ala Pro Gly Leu Leu Trp Asp Ala 35 40 45

Ser His Gln Gln Gln Pro Thr Ser Ser Ser His His Gly Gly Ala 50 60

Gly Ala Val Glu Ile Arg Ser Arg His Ser Ser Tyr Pro Ala Gly Thr

Ser Arg Ser Ala Pro Pro Asn Leu Trp Ala Ala Gln Arg Tyr Gly Arg 100 105 110

Glu Leu Arg Arg Met Ser Asp Glu Phe Val Asp Ser Phe Lys Lys Gly 115 120 125

Leu Pro Arg Pro Lys Ser Ala Gly Thr Ala Thr Gln Met Arg Gln Ser 130 135 140

Ser Ser Trp Thr Arg Val Phe Gln Ser Trp Trp Asp Arg Asn Leu Gly 145 150 155

Arg Gly Ser Ser Ala Pro Ser Gln

192 PRT

Homo sapiens

Met Asp Gly Ser Gly Glu Gln Pro Arg Gly Gly Gly Pro Thr Ser Ser 1 10 15

Glu Gln Ile Met Lys Thr Gly Ala Leu Leu Leu Gln Gly Phe Ile Gln

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asp Arg Ala Gly Arg Met Gly Gly Glu Ala Pro Glu Leu Ala Leu Asp 35 40 45 Pro Val Pro Gln Asp Ala Ser Thr Lys Lys Leu Ser Glu Cys Leu Lys 50 60 Arg Ile Gly Asp Glu Leu Asp Ser Asn Met Glu Leu Gln Arg Met Ile Ala Ala Val Asp Thr Asp Ser Pro Arg Glu Val Phe Phe Arg Val Ala 85 90 95 Ala Asp Met Phe Ser Asp Gly Asn Phe Asn Trp Gly Arg Val Ala 100 105 110 Leu Phe Tyr Phe Ala Ser Lys Leu Val Leu Lys Ala Leu Cys Thr Lys Val Pro Glu Leu Ile Arg Thr Ile Met Gly Trp Thr Leu Asp Phe Leu 130 135 140 Arg Glu Arg Leu Leu Gly Trp Ile Gln Asp Gln Gly Gly Trp Asp Gly 145 150 155 160 Leu Leu Ser Tyr Phe Gly Thr Pro Thr Trp Gln Thr Val Thr Ile Phe Val Ala Gly Val Leu Thr Ala Ser Leu Thr Ile Trp Lys Lys Met Gly

Met Ala His Ala Gly Arg Thr Gly Tyr Asp Asn Arg Glu Ile Val Met
1 10 15 Gly Asp Val Gly Ala Ala Pro Pro Gly Ala Ala Pro Ala Pro Gly Ile 35 40 45 Phe Ser Ser Gln Pro Gly His Thr Pro His Pro Ala Ala Ser Arg Asp Pro Val Ala Arg Thr Ser Pro Leu Gln Thr Pro Ala Ala Pro Gly Ala 65 70 75 80 Ala Ala Gly Pro Ala Leu Ser Pro Val Pro Pro Val Val His Leu Thr Leu Arg Gln Ala Gly Asp Asp Phe Ser Arg Arg Tyr Arg Asp Phe Ala Glu Met Ser Ser Gln Leu His Leu Thr Pro Phe Thr Ala Arg Gly 115 120 125 Arg Phe Ala Thr Val Val Glu Glu Leu Phe Arg Asp Gly Val Asn Trp

<210> 161 <211> 239 <212> PRT <213> Homo sapiens

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Gly Arg Ile Val Ala Phe Phe Glu Phe Gly Gly Val Met Cys Val Glu
145 150 155 160

Ser Val Asn Arg Glu Met Ser Pro Leu Val Asp Asn Ile Ala Leu Trp 165 170 175

Met Thr Glu Tyr Leu Asn Arg His Leu His Thr Trp Ile Gln Asp Asn 180 185 190

Gly Gly Trp Asp Ala Phe Val Glu Leu Tyr Gly Pro Ser Met Arg Pro 195 200 205

Leu Phe Asp Phe Ser Trp Leu Ser Leu Lys Thr Leu Leu Ser Leu Ala 210 220

Leu Val Gly Ala Cys Ile Thr Leu Gly Ala Tyr Leu Gly His Lys 235 235

<210> 162 <211> 160 <212> PRT <213> Homo sapiens

WO 2004/009622

Met Ser Glu Val Arg Pro Leu Ser Arg Asp Ile Leu Met Glu Thr Leu 1 5 10 15

Leu Tyr Glu Gln Leu Leu Glu Pro Pro Thr Met Glu Val Leu Gly Met 20 25 30

Thr Asp Ser Glu Glu Asp Leu Asp Pro Met Glu Asp Phe Asp Ser Leu 35 40 45

Glu Cys Met Glu Gly Ser Asp Ala Leu Ala Leu Arg Leu Ala Cys Ile 50 55 60

Gly Asp Glu Met Asp Val Ser Leu Arg Ala Pro Arg Leu Ala Gln Leu 65 70 75 80

Ser Glu Val Ala Met His Ser Leu Gly Leu Ala Phe Ile Tyr Asp Gln 85 90 95

Thr Glu Asp Ile Arg Asp Val Leu Arg Ser Phe Met Asp Gly Phe Thr $100 \ \ 105$

Thr Leu Lys Glu Asn Ile Met Arg Phe Trp Arg Ser Pro Asn Pro Gly 115 120 125

Ser Trp Val Ser Cys Glu Gln Val Leu Leu Ala Leu Leu Leu Leu Leu Leu 130 140

Ala Leu Leu Leu Pro Leu Leu Ser Gly Gly Leu His Leu Leu Lys 145 150 160

163 198 PRT

<210> <211> <212> <213>

<400> 163

Met Ala Lys Gln Pro Ser Asp Val Ser Ser Glu Cys Asp Arg Glu Gly 1 5 15

Arg Gln Leu Gln Pro Ala Glu Arg Pro Pro Gln Leu Arg Pro Gly Ala 20 25 30

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Pro Thr Ser Leu Gln Thr Glu Pro Gln Gly Asn Pro Glu Gly Asn His
35 40 45

Gly Gly Glu Gly Asp Ser Cys Pro His Gly Ser Pro Gln Gly Pro Leu Ala Pro Pro Ala Ser Pro Gly Pro Phe Ala Thr Arg Ser Pro Leu Phe 65 70 75Ile Phe Met Arg Arg Ser Ser Leu Leu Ser Arg Ser Ser Ser Gly Tyr Phe Ser Phe Asp Thr Asp Arg Ser Pro Ala Pro Met Ser Cys Asp Lys Ser Thr Gln Thr Pro Ser Pro Pro Cys Gln Ala Phe Asn His Tyr Leu 115 120 125 Ser Ala Met Ala Ser Met Arg Gln Ala Glu Pro Ala Asp Met Arg Pro Glu Ile Trp Ile Ala Gln Glu Leu Arg Arg Ile Gly Asp Glu Phe Asn 145 150 160 Ala Tyr Tyr Ala Arg Arg Val Phe Leu Asn Asn Tyr Gln Ala Ala Glu 165 170 175 Asp His Pro Arg Met Val Ile Leu Arg Leu Leu Arg Tyr Ile Val Arg

<210> <211> <212> 164 404

PRT Homo sapiens

Leu Val Trp Arg Met His 195

<400> 164

Met Glu Ala Gly Glu Glu Pro Leu Leu Ala Glu Leu Lys Pro Gly

Arg Pro His Gln Phe Asp Trp Lys Ser Ser Cys Glu Thr Trp Ser Val

Ala Phe Ser Pro Asp Gly Ser Trp Phe Ala Trp Ser Gln Gly His Cys

Ile Val Lys Leu Ile Pro Trp Pro Leu Glu Glu Gln Phe Ile Pro Lys

Gly Phe Glu Ala Lys Ser Arg Ser Ser Lys Asn Glu Thr Lys Gly Arg 65 70 75 80

Gly Ser Pro Lys Glu Lys Thr Leu Asp Cys Gly Gln Ile Val Trp Gly

Leu Ala Phe Ser Pro Trp Pro Ser Pro Pro Ser Arg Lys Leu Trp Ala

Arg His His Pro Gln Val Pro Asp Val Ser Cys Leu Val Leu Ala Thr

Gly Leu Asn Asp Gly Gln Ile Lys Ile Trp Glu Val Gln Thr Gly Leu 130 140

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Leu Leu Asn Leu Ser Gly His Gln Asp Val Val Arg Asp Leu Ser 145 150 160 Phe Thr Pro Ser Gly Ser Leu Ile Leu Val Ser Ala Ser Arg Asp Lys 165 170 175Thr Leu Arg Ile Trp Asp Leu Asn Lys His Gly Lys Gln Ile Gln Val 180 185 190 Leu Ser Gly His Leu Gln Trp Val Tyr Cys Cys Ser Ile Ser Pro Asp $195 \hspace{1.5cm} 200 \hspace{1.5cm} 205$ Cys Ser Met Leu Cys Ser Ala Ala Gly Glu Lys Ser Val Phe Leu Trp 210 215 Ser Met Arg Ser Tyr Thr Leu Ile Arg Lys Leu Glu Gly His Gln Ser 225 230 240 Ser Val Val Ser Cys Asp Phe Ser Pro Asp Ser Ala Leu Leu Val Thr 245 250 255 Ala Ser Tyr Asp Thr Asn Val Ile Met Trp Asp Pro Tyr Thr Gly Glu 260 265 270 Arg Leu Arg Ser Leu His His Thr Gln Val Asp Pro Ala Met Asp Asp 275 280 285 Ser Asp Val His Ile Ser Ser Leu Arg Ser Val Cys Phe Ser Pro Glu 290 295 300 Gly Leu Tyr Leu Ala Thr Val Ala Asp Asp Arg Leu Leu Arg Ile Trp 305 310 315 Ala Leu Glu Leu Lys Thr Pro Ile Ala Phe Ala Pro Met Thr Asn Gly Leu Cys Cys Thr Phe Phe Pro His Gly Gly Val Ile Ala Thr Gly Thr Arg Asp Gly His Val Gln Phe Trp Thr Ala Pro Arg Val Leu Ser Ser 355 360 365 Leu Lys His Leu Cys Arg Lys Ala Leu Arg Ser Phe Leu Thr Thr Tyr 370 375 380Gln Val Leu Ala Leu Pro Ile Pro Lys Lys Met Lys Glu Phe Leu Thr 385 390 395 400

<210> 165
<211> 1453

Tyr Arg Thr Phe

∠400<u>></u> 165

Met Ile Lys Cys Leu Ser Val Glu Val Gln Ala Lys Leu Arg Ser Gly 1 10 15

Leu Ala Ile Ser Ser Leu Gly Gln Cys Val Glu Glu Leu Ala Leu Asn 20 25 30

Ser Ile Asp Ala Glu Ala Lys Cys Val Ala Val Arg Val Asn Met Glu 35 40 45

<212> PRT <213> Homo sapiens

protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Thr Phe Gln Val Gln Val Ile Asp Asn Gly Phe Gly Met Gly Ser Asp Asp Val Glu Lys Val Gly Asn Arg Tyr Phe Thr Ser Lys Cys His Ser 65 70 75 80Val Gln Asp Leu Glu Asn Pro Arg Phe Tyr Gly Phe Arg Gly Glu Ala 85 90 95 Leu Ala Asn Ile Ala Asp Met Ala Ser Ala Val Glu Ile Ser Ser Lys 100 105 110Lys Asn Arg Thr Met Lys Thr Phe Val Lys Leu Phe Gln Ser Gly Lys 115 120 125 Ala Leu Lys Ala Cys Glu Ala Asp Val Thr Arg Ala Ser Ala Gly Thr 130 140 Thr Val Thr Val Tyr Asn Leu Phe Tyr Gln Leu Pro Val Arg Arg Lys Cys Met Asp Pro Arg Leu Glu Phe Glu Lys Val Arg Gln Arg Ile Glu 165 170 175 Ala Leu Ser Leu Met His Pro Ser Ile Ser Phe Ser Leu Arg Asn Asp 180 185 190 Val Ser Gly Ser Met Val Leu Gln Leu Pro Lys Thr Lys Asp Val Cys 195 200 205 Ser Arg Phe Cys Gln Ile Tyr Gly Leu Gly Lys Ser Gln Lys Leu Arg Glu Ile Ser Phe Lys Tyr Lys Glu Phe Glu Leu Ser Gly Tyr Ile Ser 225 230 235 240 Ser Glu Ala His Tyr Asn Lys Asn Met Gln Phe Leu Phe Val Asn Lys 245 250 255 Arg Leu Val Leu Arg Thr Lys Leu His Lys Leu Ile Asp Phe Leu Leu 260 265 270 Arg Lys Glu Ser Ile Ile Cys Lys Pro Lys Asn Gly Pro Thr Ser Arg 275 280 285 Gln Met Asn Ser Ser Leu Arg His Arg Ser Thr Pro Glu Leu Tyr Gly 290 295 300 Ile Tyr Val Ile Asn Val Gln Cys Gln Phe Cys Glu Tyr Asp Val Cys 305 310 315 320 Met Glu Pro Ala Lys Thr Leu Ile Glu Phe Gln Asn Trp Asp Thr Leu 325 330 335 Leu Phe Cys Ile Gln Glu Gly Val Lys Met Phe Leu Lys Gln Glu Lys 340 345 350 Leu Phe Val Glu Leu Ser Gly Glu Asp Ile Lys Glu Phe Ser Glu Asp 355 360 365 Asn Gly Phe Ser Leu Phe Asp Ala Thr Leu Gln Lys Arg Val Thr Ser

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asp Glu Arg ser Asn Phe Gln Glu Ala Cys Asn Asn Ile Leu Asp Ser 385 390 395 400

Tyr Glu Met Phe Asn Leu Gln Ser Lys Ala Val Lys Arg Lys Thr Thr 405 410 415 Ala Glu Asn Val Asn Thr Gln Ser Ser Arg Asp Ser Glu Ala Thr Arg 420 425 430 Lys Asn Thr Asn Asp Ala Phe Leu Tyr Ile Tyr Glu Ser Gly Gly Pro
435 440 445 Gly His Ser Lys Met Thr Glu Pro Ser Leu Gln Asn Lys Asp Ser Ser 450 455 460 Cys Ser Glu Ser Lys Met Leu Glu Gln Glu Thr Ile Val Ala Ser Glu 465 470 475 480 Ala Gly Glu Asn Glu Lys His Lys Lys Ser Phe Leu Glu His Ser Ser 490 495 Leu Glu Asn Pro Cys Gly Thr Ser Leu Glu Met Phe Leu Ser Pro Phe 500 510 Gln Thr Pro Cys His Phe Glu Glu Ser Gly Gln Asp Leu Glu Ile Trp 515 520 525 Lys Glu Ser Thr Thr Val Asn Gly Met Ala Ala Asn Ile Leu Lys Asn 530 535 540 Asn Arg Ile Gln Asn Gln Pro Lys Arg Phe Lys Asp Ala Thr Glu Val 545 550 555 Gly Cys Gln Pro Leu Pro Phe Ala Thr Thr Leu Trp Gly Val His Ser Ala Gln Thr Glu Lys Glu Lys Lys Lys Glu Ser Ser Asn Cys Gly Arg Arg Asn Val Phe Ser Tyr Gly Arg Val Lys Leu Cys Ser Thr Gly Phe 595 600 605Ile Thr His Val Val Gln Asn Glu Lys Thr Lys Ser Thr Glu Thr Glu 610 615 620His Ser Phe Lys Asn Tyr Val Arg Pro Gly Pro Thr Arg Ala Gln Glu 625 630 635 640 Thr Phe Gly Asn Arg Thr Arg His Ser Val Glu Thr Pro Asp Ile Lys 655 Asp Leu Ala Ser Thr Leu Ser Lys Glu Ser Gly Gln Leu Pro Asn Lys Lys Asn Cys Arg Thr Asn Ile Ser Tyr Gly Leu Glu Asn Glu Pro Thr 675 680 685 Ala Thr Tyr Thr Met Phe Ser Ala Phe Gln Glu Gly Ser Lys Lys Ser Gln Thr Asp Cys Ile Leu Ser Asp Thr Ser Pro Ser Phe Pro Trp Tyr 705 710 720Arg His Val Ser Asn Asp Ser Arg Lys Thr Asp Lys Leu Ile Gly Phe 725 730 735



protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Lys Pro Ile Val Arg Lys Lys Leu Ser Leu Ser Ser Gln Leu Gly 740 745 750 Ser Leu Glu Lys Phe Lys Arg Gln Tyr Gly Lys Val Glu Asn Pro Leu 755 760 765 Asp Thr Glu Val Glu Glu Ser Asn Gly Val Thr Thr Asn Leu Ser Leu 770 780 Gln Val Glu Pro Asp Ile Leu Leu Lys Asp Lys Asn Arg Leu Glu Asn 785 790 795 Ser Asp Val Cys Lys Ile Thr Thr Met Glu His Ser Asp Ser Asp Ser 805 810 815 Ser Cys Gln Pro Ala Ser His Ile Leu Asp Ser Glu Lys Phe Pro Phe 820 825 830 Ser Lys Asp Glu Asp Cys Leu Glu Gln Gln Met Pro Ser Leu Arg Glu 840 845 Ser Pro Met Thr Leu Lys Glu Leu Ser Leu Phe Asn Arg Lys Pro Leu 850 860 Asp Leu Glu Lys Ser Ser Glu Ser Leu Ala Ser Lys Leu Ser Arg Leu 865 870 875 Lys Gly Ser Glu Arg Glu Thr Gln Thr Met Gly Met Met Ser Arg Phe 885 890 Asn Glu Leu Pro Asn Ser Asp Ser Ser Arg Lys Asp Ser Lys Leu Cys 900 905 910Ser Val Leu Thr Gln Asp Phe Cys Met Leu Phe Asn Asn Lys His Glu 915 925 Lys Thr Glu Asn Gly Val Ile Pro Thr Ser Asp Ser Ala Thr Gln Asp 930 935 940 Asn Ser Phe Asn Lys Asn Ser Lys Thr His Ser Asn Ser Asn Thr Thr 945 950 955 Glu Asn Cys Val Ile Ser Glu Thr Pro Leu Val Leu Pro Tyr Asn Asn 965 970 975 Ser Lys Val Thr Gly Lys Asp Ser Asp Val Leu Ile Arg Ala Ser Glu 980 985 990 Gin Gin Tie Gly Ser Leu Asp Ser Pro Ser Gly Met Leu Met Asn Pro 995 1000 1005 Val Glu Asp Ala Thr Gly Asp Gln Asn Gly Ile Cys Phe Gln Ser 1010 1020 Glu Glu Ser Lys Ala Arg Ala Cys Ser Glu Thr Glu Glu Ser Asn 1025 1030 Thr Cys Cys Ser Asp Trp Gln Arg His Phe Asp Val Ala Leu Gly 1040 1050 Arg Met Val Tyr Val Asn Lys Met Thr Gly Leu Ser Thr Phe Ile 1055 1060 1065

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ala Pro Thr Glu Asp Ile Gln Ala Ala Cys Thr Lys Asp Leu Thr
1070 1075 1080

Thr Val Ala Val Asp Val Val Leu Glu Asn Gly Ser Gln Tyr Arg 1085 1090 1095 Cys Gln Pro Phe Arg Ser Asp Leu Val Leu Pro Phe Leu Pro Arg 1100 1110 1110 Ala Arg Ala Glu Arg Thr Val Met Arg Gln Asp Asn Arg Asp Thr 1115 1120 1125 Val Asp Asp Thr Val Ser Ser Glu Ser Leu Gln Ser Leu Phe Ser 1130 1140 Glu Trp Asp Asn Pro Val Phe Ala Arg Tyr Pro Glu Val Ala Val 1145 1150 1155 Asp Val Ser Ser Gly Gln Ala Glu Ser Leu Ala Val Lys Ile His 1160 1165 1170 Asn Ile Leu Tyr Pro Tyr Arg Phe Thr Lys Gly Met Ile His Ser Met Gln Val Leu Gln Gln Val Asp Asn Lys Phe Ile Ala Cys Leu 1190 1200 Met Ser Thr Lys Thr Glu Glu Asn Gly Glu Ala Gly Gly Asn Leu 1205 1210 1215 Leu Val Leu Val Asp Gln His Ala Ala His Glu Arg Ile Arg Leu 1220 1230 Glu Gln Leu Ile Ile Asp Ser Tyr Glu Lys Gln Gln Ala Gln Gly 1235 1240 1245 Ser Gly Arg Lys Leu Leu Ser Ser Thr Leu Ile Pro Pro Leu 1250 1260 Glu Ile Thr Val Thr Glu Glu Gln Arg Arg Leu Leu Trp Cys Tyr 1265 1270 1275 His Lys Asn Leu Glu Asp Leu Gly Leu Glu Phe Val Phe Pro Asp 1280 1285 1290 Thr Ser Asp Ser Leu Val Leu Val Gly Lys Val Pro Leu Cys Phe 1295 1300 1305 Val Glu Arg Glu Ala Asn Glu Leu Arg Arg Gly Arg Ser Thr Val 1310 1320 1320 Thr Lys Ser Ile Val Glu Glu Phe Ile Arg Glu Gln Leu Glu Leu 1325 1330 1335 Leu Gln Thr Thr Gly Gly Ile Gln Gly Thr Leu Pro Leu Thr Val 1340 1350 Gln Lys Val Leu Ala Ser Gln Ala Cys His Gly Ala Ile Lys Phe 1355 1360 1365 Asn Asp Gly Leu Ser Leu Gln Glu Ser Cys Arg Leu Ile Glu Ala 1370 1380 Leu Ser Ser Cys Gln Leu Pro Phe Gln Cys Ala His Gly Arg Pro 1385 1390 1395

PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ser Met Leu Pro Leu Ala Asp Ile Asp His Leu Glu Gln Glu Lys 1400 1410

Gln Ile Lys Pro Asn Leu Thr Lys Leu Arg Lys Met Ala Gln Ala 1415 1420 1425

Trp Arg Leu Phe Gly Lys Ala Glu Cys Asp Thr Arg Gln Ser Leu 1430 1440

Gln Gln Ser Met Pro Pro Cys Glu Pro Pro 1445 1450

<210> 166 <211> 135 <212> PRT <213> Homo sapiens

Ser Asn Val Pro His Lys Ser Ser Leu Pro Glu Gly Ile Arg Pro Gly
1 10 15

Thr Val Leu Arg Ile Arg Gly Leu Val Pro Pro Asn Ala Ser Arg Phe 20 25 30

His Val Asn Leu Leu Cys Gly Glu Glu Gln Gly Ser Asp Ala Ala Leu 35 40 45

His Phe Asn Pro Arg Leu Asp Thr Ser Glu Val Val Phe Asn Ser Lys 50 60

Glu Gln Gly Ser Trp Gly Arg Glu Glu Arg Gly Pro Gly Val Pro Phe

Gln Arg Gly Gln Pro Phe Glu Val Leu Ile Ile Ala Ser Asp Asp Gly 85 90 95

Phe Lys Ala Val Val Gly Asp Ala Gln Tyr His His Phe Arg His Arg 100 105 110

Leu Pro Leu Ala Arg Val Arg Leu Val Glu Val Gly Gly Asp Val Gln
115 120 125

Leu Asp Ser Val Arg Ile Phe 130 135

<210> 167 <211> 373 <212> PRT <213> Homo sapiens

Met Thr Thr Ser Ala Ser Ser His Leu Asn Lys Gly Ile Lys Gln Val 1 5 10 15

Tyr Met Ser Leu Pro Gln Gly Glu Lys Val Gln Ala Met Tyr Ile Trp

Ile Asp Gly Thr Gly Glu Gly Leu Arg Cys Lys Thr Arg Thr Leu Asp 35 40 45

Ser Glu Pro Lys Cys Val Glu Glu Leu Pro Glu Trp Asn Phe Asp Gly 50 60

Ser Ser Thr Leu Gln Ser Glu Gly Ser Asn Ser Asp Met Tyr Leu Val



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Pro Ala Ala Met Phe Arg Asp Pro Phe Arg Lys Asp Pro Asn Lys Leu Val Leu Cys Glu Val Phe Lys Tyr Asn Arg Arg Pro Ala Glu Thr Asn 100 105 110 Leu Arg His Thr Cys Lys Arg Ile Met Asp Met Val Ser Asn Gln His Pro Trp Phe Gly Met Glu Gln Glu Tyr Thr Leu Met Gly Thr Asp Gly 130 135 140 His Pro Phe Gly Trp Pro Ser Asn Gly Phe Pro Gly Pro Gln Gly Pro 145 150 160 Tyr Tyr Cys Gly Val Gly Ala Asp Arg Ala Tyr Gly Arg Asp Ile Val 165 170 175 Glu Ala His Tyr Arg Ala Cys Leu Tyr Ala Gly Val Lys Ile Ala Gly 180 185 Thr Asn Ala Glu Val Met Pro Ala Gln Trp Glu Phe Gln Ile Gly Pro 195 200 205 Leu His Arg Val Cys Glu Asp Phe Gly Val Ile Ala Thr Phe Asp Pro 225 230 240 Lys Pro Ile Pro Gly Asn Trp Asn Gly Ala Gly Cys His Thr Asn Phe 245 250 255Ser Thr Lys Ala Met Arg Glu Glu Asn Gly Leu Lys Tyr Ile Glu Glu 265 270 Ala Ile Glu Lys Leu Ser Lys Arg His Gln Tyr His Ile Arg Ala Tyr 275 280 285 Asp Pro Lys Gly Gly Leu Asp Asn Ala Arg Arg Leu Thr Gly Phe His $290 \hspace{1cm} 295 \hspace{1cm} 300$ Glu Thr Ser Asn Ile Asn Asp Phe Ser Ala Gly Val Ala Asn Arg Ser 305 310 315 Ala Ser Ile Arg Ile Pro Arg Thr Val Gly Gln Glu Lys Lys Gly Tyr Phe Glu Asp Arg Arg Pro Ser Ala Asn Cys Asp Pro Phe Ser Val Thr 340 345Glu Ala Leu Ile Arg Thr Cys Leu Leu Asn Glu Thr Gly Asp Glu Pro Phe Gln Tyr Lys Asn

<210> 168 <211> 387

<213> Homo sapiens

<400> 168

Met Pro Gly His Leu Gln Glu Gly Phe Gly Cys val Val Thr Asn Arg

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Phe Asp Gln Leu Phe Asp Asp Glu Ser Asp Pro Phe Glu Val Leu Lys Ala Ala Glu Asn Lys Lys Glu Ala Gly Gly Gly Gly Val Gly Gly 45Pro Gly Ala Lys Ser Ala Ala Gln Ala Ala Ala Gln Thr Asn Ser Asn 50 60 Ala Ala Gly Lys Gln Leu Arg Lys Glu Ser Gln Lys Asp Arg Lys Asn 65 70 80 Pro Leu Pro Pro Ser Val Gly Val Val Asp Lys Lys Glu Glu Thr Gln 90 95 Pro Pro Val Ala Leu Lys Lys Glu Gly Ile Arg Arg Val Gly Arg Arg 100 105 Pro Asp Gln Gln Leu Gln Gly Glu Gly Lys Ile Ile Asp Arg Arg Pro 115 120 125 Glu Arg Arg Pro Pro Arg Glu Arg Arg Phe Glu Lys Pro Leu Glu Glu 130 140 Lys Gly Glu Gly Glu Phe Ser Val Asp Arg Pro Ile Ile Asp Arg 145 150 160 Pro Ile Arg Gly Arg Gly Gly Leu Gly Arg Gly Arg Gly Gly Arg Gly 175 Arg Gly Met Gly Arg Gly Asp Gly Phe Asp Ser Arg Gly Lys Arg Glu 185 190 Phe Asp Arg His Ser Gly Ser Asp Arg Ser Gly Leu Lys His Glu Asp 195 200 205 Lys Arg Gly Gly Ser Gly Ser His Asn Trp Gly Thr Val Lys Asp Glu 210 215 220 Leu Thr Asp Leu Asp Gln Ser Asn Val Thr Glu Glu Thr Pro Glu Gly 225 230 235 240 Glu Glu His His Pro Val Ala Asp Thr Glu Asn Lys Glu Asn Glu Val 245 250 255 Glu Glu Val Lys Glu Glu Gly Pro Lys Glu Met Thr Leu Asp Glu Trp 260 265 270 Lys Ala Ile Gln Asn Lys Asp Arg Ala Lys Val Glu Phe Asn Ile Arg 275 280 285 Lys Pro Asn Glu Gly Ala Asp Gly Gln Trp Lys Lys Gly Phe Val Leu 290 295 300 His Lys Ser Lys Ser Glu Glu Ala His Ala Glu Asp Ser Val Met Asp 305 310 315 320 His His Phe Arg Lys Pro Ala Asn Asp Ile Thr Ser Gln Leu Glu Ile 325 330 335 Asn Phe Gly Asp Leu Gly Arg Pro Gly Arg Gly Gly Arg Gly Gly Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gly Gly Arg Gly Arg Gly Gly Arg Pro Asn Arg Gly Ser Arg Thr Asp

Lys Ser Ser Ala Ser Ala Pro Asp Val Asp Asp Pro Glu Ala Phe Pro 370 380

Ala Leu Ala 385

169 894

PRT Homo sapiens

<400> 169

Met Arg Pro Met Arg Ile Phe Val Asn Asp Asp Arg His Val Met Ala

Lys His Ser Ser Val Tyr Pro Thr Gln Glu Glu Leu Glu Ala Val Gln
20 25 30

Asn Met Val Ser His Thr Glu Arg Ala Leu Lys Ala Val Ser Asp Trp $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ile Asp Glu Gln Glu Lys Gly Ser Ser Glu Gln Ala Glu Ser Asp Asn 50 . 60

Met Asp Val Pro Pro Glu Asp Asp Ser Lys Glu Gly Ala Gly Glu Gln 65 70 80

Lys Thr Glu His Met Thr Arg Thr Leu Arg Gly Val Met Arg Val Gly 95

Leu Val Ala Lys Cys Leu Leu Leu Lys Gly Asp Leu Asp Leu Glu Leu $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$

Val Leu Leu Cys Lys Glu Lys Pro Thr Thr Ala Leu Leu Asp Lys Val

Ala Asp Asn Leu Ala Ile Gln Leu Ala Ala Val Thr Glu Asp Lys Tyr 130 135 140

Glu Ile Leu Gln Ser Val Asp Asp Ala Ala Ile Val Ile Lys Asn Thr 145 150 160

Lys Glu Pro Pro Leu Ser Leu Thr Ile His Leu Thr Ser Pro Val Val 165 170 175

Arg Glu Glu Met Glu Lys Val Leu Ala Gly Glu Thr Leu Ser Val Asn 180 185 190

Asp Pro Pro Asp Val Leu Asp Arg Gln Lys Cys Leu Ala Ala Leu Ala

Ser Leu Arg His Ala Lys Trp Phe Gln Ala Arg Ala Asn Gly Leu Lys 210 215 220

Ser Cys Val Ile Val Ile Arg Val Leu Arg Asp Leu Cys Thr Arg Val 225 230 235 240

Pro Thr Trp Gly Pro Leu Arg Gly Trp Pro Leu Glu Leu Leu Cys Glu 245 250 255

Lys Ser Ile Gly Thr Ala Asn Arg Pro Met Gly Ala Gly Glu Ala Leu 260 265 270

Protein complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Arg Arg Val Leu Glu Cys Leu Ala Ser Gly Ile Val Met Pro Asp Gly 275 280 285 Ser Gly Ile Tyr Asp Pro Cys Glu Lys Glu Ala Thr Asp Ala Ile Gly His Leu Asp Arg Gln Gln Arg Glu Asp Ile Thr Gln Ser Ala Gln His Ala Leu Arg Leu Ala Ala Phe Gly Gln Leu His Lys Val Leu Gly Met 325 330 335 Asp Pro Leu Pro Ser Lys Met Pro Lys Lys Pro Lys Asn Glu Asn Pro 340 345 val Asp Tyr Thr Val Gln Ile Pro Pro Ser Thr Thr Tyr Ala Ile Thr Pro Met Lys Arg Pro Met Glu Glu Asp Gly Glu Glu Lys Ser Pro Ser 370 380 Lys Lys Lys Lys Lys Ile Gln Lys Lys Glu Glu Lys Ala Glu Pro Pro 385 390 395 400 Gln Ala Met Asn Ala Leu Met Arg Leu Asn Gln Leu Lys Pro Gly Leu 405 410 415 Gln Tyr Lys Leu Val Ser Gln Thr Gly Pro Val His Ala Pro Ile Phe Thr Met Ser Val Glu Val Asp Gly Asn Ser Phe Glu Ala Ser Gly Pro 435 440 445 Ser Lys Lys Thr Ala Lys Leu His Val Ala Val Lys Val Leu Gln Asp 450 455 460 Met Gly Leu Pro Thr Gly Ala Glu Gly Arg Asp Ser Ser Lys Gly Glu 465 470 475 480 Asp Ser Ala Glu Glu Thr Glu Ala Lys Pro Ala Val Ala Pro Ala 485 490 495 Pro Val Val Glu Ala Val Ser Thr Pro Ser Ala Ala Phe Pro Ser Asp 500 505 510 Ala Thr Ala Glu Gln Gly Pro Ile Leu Thr Lys His Gly Lys Asn Pro 515 520 525 Val Met Glu Leu Asn Glu Lys Arg Arg Gly Leu Lys Tyr Glu Leu Ile 530 540 Ser Glu Thr Gly Gly Ser His Asp Lys Arg Phe Val Met Glu Val Glu 545 550 560 555 Val Asp Gly Gln Lys Phe Gln Gly Ala Gly Ser Asn Lys Lys Val Ala Lys Ala Tyr Ala Ala Leu Ala Ala Leu Glu Lys Leu Phe Pro Asp Thr 580 585 590 Pro Leu Ala Leu Asp Ala Asn Lys Lys Lys Arg Ala Pro Val Pro Val 595 600 605

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Arg Gly Gly Pro Lys Phe Ala Ala Lys Pro His Asn Pro Gly Phe Gly
610 615 620

Met Gly Gly Pro Met His Asn Glu Val Pro Pro Pro Pro Asn Leu Arg 625 630 635 Gly Arg Gly Arg Gly Ser Ile Arg Gly Arg Gly Arg Gly Arg Gly 655 650Phè Gly Gly Ala Asn His Gly Gly Tyr Met Asn Ala Gly Ala Gly Tyr 660 665 670 Gly Ser Tyr Gly Tyr Gly Gly Asn Ser Ala Thr Ala Gly Tyr Ser Gln 685 Phe Tyr Ser Asn Gly Gly His Ser Gly Asn Ala Ser Gly Gly Gly Gly Gly 690 700 Gly Gly Gly Gly Ser ser Gly Tyr Gly Ser Tyr Tyr Gln Gly Asp 705 $\,$ 710 $\,$ 720 $\,$ Asn Tyr Asn Ser Pro Val Pro Pro Lys His Ala Gly Lys Lys Gln Pro 725 730 735 His Gly Gly Gln Gln Lys Pro Ser Tyr Gly Ser Gly Tyr Gln Ser His 740 745Gln Gly Gln Gln Ser Tyr Asn Gln Ser Pro Tyr Ser Asn Tyr Gly 765 760 765 Pro Pro Gln Gly Lys Gln Lys Gly Tyr Asn His Gly Gln Gly Ser Tyr 770 780 Ser Tyr Ser Asn Ser Tyr Asn Ser Pro Gly Gly Gly Gly Gly Ser Asp 785 790 795 Tyr Asn Tyr Glu Ser Lys Phe Asn Tyr Ser Gly Ser Gly Gly Arg Ser 815 Gly Gly Asn Ser Tyr Gly Ser Gly Gly Ala Ser Tyr Asn Pro Gly Ser 820 825 His Gly Gly Tyr Gly Gly Gly Ser Gly Gly Gly Ser Ser Tyr Gln Gly 835 840 845 Lys Gln Gly Gly Tyr Ser Gln Ser Asn Tyr Asn Ser Pro Gly Ser Gly $850 \ \ 850 \ \ \ 860$ Gln Asn Tyr Ser Gly Pro Pro Ser Ser Tyr Gln Ser Ser Gln Gly Gly 865 870 880 Tyr Gly Arg Asn Ala Asp His Ser Met Asn Tyr Gln Tyr Arg 885

Met Ile Ser Ser Ser Ser Val His Ser Arg Thr Phe Asn Thr Ser Asn 1 10 15

Ala Leu Gly Pro Val Cys Lys His Lys Lys Pro Leu Ser Ala Ala Lys

<210> <211> <212>

Homo sapiens

<400> 170

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ala Cys Ile Ser Glu Ile Leu Pro Ser Lys Phe Lys Pro Arg Leu Ser
35 40 45

Ala Pro Ser Ala Leu Leu Gln Glu Gln Lys Ser Ile Leu Leu Pro Ser 50 60 Glu Lys Ala Gln Ser Cys Glu Asn Leu Cys Val Ser Gly Ser Leu Asn 65 70 75 Asp Ser Lys Arg Gly Leu Pro Leu Gln Val Gly Gly Ser Ile Glu Asn 90 95 Leu Leu Met Arg Ser Arg Arg Asp Tyr Asp Ser Lys Ser Ser Ser Thr $100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}$ Met Ser Leu Gln Glu Tyr Ser Thr Ser Gly Arg Arg Pro Cys Pro Leu 115 125 125Ser Arg Lys Ala Gly Met Gln Phe Thr Met Leu Tyr Arg Asp Met His $130 \hspace{1cm} 135 \hspace{1cm} 140 \hspace{1cm}$ Gln Ile Asn Arg Ser Gly Leu Phe Leu Gly Ser Ile Ser Ser Ser 145 150 155 160 Ser Val Arg Asp Leu Ala Ser His Phe Glu Lys Ser Ser Leu Ala Leu 165 170 175 Ser Arg Gly Glu Leu Gly Pro Ser Gln Glu Gly Ser Glu His Ile Pro 180 185 190 Lys His Thr Val Ser Ser Arg Ile Thr Ala Phe Glu Gln Leu Ile Gln 195 200 205 Arg Ser Arg Ser Met Pro Ser Leu Asp Leu Ser Gly Arg Leu Ser Lys 210 210 Arg Leu Ser Lys Ser Pro Thr Pro Val Leu Ser Arg Gly Ser Leu Thr Ser Ala Arg Ser 225 230 235 Ala Glu Ser Leu Leu Glu Ser Thr Lys Leu His Pro Lys Glu Met Asp 255 Gly Met Asn Ser Ser Gly Val Tyr Ala Ser Pro Thr Cys Ser Asn Met 260 265 . 270Ala His His Ala Leu Ser Phe Arg Gly Leu Val Pro Ser Glu Pro Leu 275 280 285 Ser Thr Cys Ser Asp Asp Val Asp Arg Cys Ser Asn Ile Ser Thr Asp 290 300 Ser Arg Glu Gly Ser Gly Gly Ser Val His Gly Asp Phe Pro Lys His 305 310 315 Arg Leu Asn Lys Cys Lys Gly Thr Cys Pro Ala Ser Tyr Thr Arg Phe 325 330 335 Thr Thr Ile Arg Lys His Glu Gln Gln Gln Thr Ser Arg Gln Pro Glu 340 345 Trp Arg Leu Asp Ala Arg Gly Asp Lys Ser Thr Leu Leu Arg Asn Ile 355 360 365 Tyr Leu Met Ser Pro Leu Pro Phe Arg Leu Lys Lys Pro Leu His His

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 370 375 380

His Pro Arg Gln Pro Ser Pro Gly Asp Ser Ser Gly Leu Leu Val Gly 385 390 395 400 Gln Lys Pro Asp Leu Pro Ser Gln Pro His Gln Asp Gln Pro Pro Ser 405 410 415 Gly Gly Lys Pro Val Val Pro Thr Arg Leu Ser Ser Arg His Thr Met $420 \hspace{1cm} 425 \hspace{1cm} 430$ Ala Arg Leu Ser Arg Ser Ser Glu Pro Ser Gln Glu Arg Pro Thr Ala $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445$ Leu Glu Asp Tyr Pro Arg Ala Ile Asn Asn Gly Asn Ser Val Pro Tyr 450 455 460 Ser Asp His Ser Leu Asp Arg Asn Asn Asn Pro Gln Ser Glu Leu Ala Pro Ser Arg Gly Gly Gly Ile Leu Cys Val Cys Leu Val Ser Pro Ala 485 490 495 Arg Pro Ser Thr Leu Leu Ala Leu Ser Arg Pro Pro Leu Cys Pro Trp 500 505 Cys Ser Phe Ser Gly Leu Ser Phe Val Phe Cys Leu Phe Cys Leu Ala 515 Ile Asn His Gly Ser

<210> 171 <211> 379 <212> PRT <213> Homo sapiens

Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu Asp Leu Phe 1 10 15 Leu Ala Leu Ser Glu Asn Asn Pro Ala Gly Asn Ile Phe Ile Ser Pro Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly Thr Arg Gly 35 40 45Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn Thr Val Glu Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile Asn Lys Arg 65 70 75 80 Gly Ala Ser Tyr Ile Leu Lys Leu Ala Asn Arg Leu Tyr Gly Glu Lys $90 \hspace{1.5cm} 95$ Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln Lys Thr Tyr Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser Glu Asp Ala 115 120 125 Arg Lys Thr Ile Asn Glm Trp Val Lys Gly Gln Thr Glu Gly Lys Ile 130 135 140

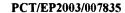
PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Pro Glu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val
145 150 155 160

Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg 180 185 190 Lys Thr Val Lys Met Met Tyr Gln Lys Lys Lys Phe Ala Tyr Gly Tyr 195 200 205 Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser Thr Gly Leu Lys Lys Ile Glu Glu Glu Leu Thr Leu Glu Lys Leu His 245 250 255 Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn Val Ser Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu 275 280 285 Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His 305 310 315 320 Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala 335 Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn Phe Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser Gly 355 360 365 Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro

Met Ala Leu Leu Val Leu Gly Leu Val Ser Cys Thr Phe Phe Leu Ala Val Asn Gly Leu Tyr Ser Ser Ser Asp Asp Val Ile Glu Leu Thr Pro Ser Asn Phe Asn Arg Glu Val Ile Gln Ser Asp Ser Leu Trp Leu Val Glu Phe Tyr Ala Pro Trp Cys Gly His Cys Gln Arg Leu Thr Pro Glu Trp Lys Lys Ala Ala Thr Ala Leu Lys Asp Val Val Lys Val Gly Ala

<210> 172 <211> 440 <212> PRT <213> Homo sapiens



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Val Asp Ala Asp Lys His His Ser Leu Gly Gly Gln Tyr Gly Val Gln

85 90 95

Gly Phe Pro Thr Ile Lys Ile Phe Gly Ser Asn Lys Asn Arg Pro Glu Asp Tyr Gln Gly Gly Arg Thr Gly Glu Ala Ile Val Asp Ala Ala Leu Ser Ala Leu Arg Gln Leu Val Lys Asp Arg Leu Gly Gly Arg Ser Gly 130 135 140 Gly Tyr Ser Ser Gly Lys Gln Gly Arg Ser Asp Ser Ser Ser Lys Lys 145 150 155 160 Asp Val Ile Glu Leu Thr Asp Asp Ser Phe Asp Lys Asn Val Leu Asp $170 \ 170 \ 175$ Ser Glu Asp Val Trp Met Val Glu Phe Tyr Ala Pro Trp Cys Gly His 180 185 190 Cys Lys Asn Leu Glu Pro Glu Trp Ala Ala Ala Ser Glu Val Lys 195 200 205 Glu Gln Thr Lys Gly Lys Val Lys Leu Ala Ala Val Asp Ala Thr Val 210 225 220 Asn Gln Val Leu Ala Ser Arg Tyr Gly Ile Arg Gly Phe Pro Thr Ile 225 230 235 240 Lys Ile Phe Gln Lys Gly Glu Ser Pro Val Asp Tyr Asp Gly Gly Arg 245 250 Thr Arg Ser Asp Ile Val Ser Arg Ala Leu Asp Leu Phe Ser Asp Asn 260 265 270 Ala Pro Pro Glu Leu Leu Glu Ile Ile Asn Glu Asp Ile Ala Lys 275 280 285 Arg Thr Cys Glu Glu His Gln Leu Cys Val Val Ala Val Leu Pro His 290 300 Ile Leu Asp Thr Gly Ala Ala Gly Arg Asn Ser Tyr Leu Glu Val Leu 305 310 315 320 Leu Lys Leu Ala Asp Lys Tyr Lys Lys Lys Met Trp Gly Trp Leu Trp Thr Glu Ala Gly Ala Gln Ser Glu Leu Glu Thr Ala Leu Gly Ile Gly 340 350 Gly Phe Gly Tyr Pro Ala Met Ala Ala Ile Asn Ala Arg Lys Met Lys 355 360 365 Phe Ala Leu Leu Lys Gly Ser Phe Ser Glu Gln Gly Ile Asn Glu Phe 370 380 Leu Arg Glu Leu Ser Phe Gly Arg Gly Ser Thr Ala Pro Val Gly Gly 385 390 395 400 Gly Ala Phe Pro Thr Ile Val Glu Arg Glu Pro Trp Asp Gly Arg Asp 405 410 415 Gly Glu Leu Pro Val Glu Asp Asp Ile Asp Leu Ser Asp Val Glu Leu Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asp Asp Leu Gly Lys Asp Glu Leu 435 440

<210> 173 <211> 193 <212> PRT

Homo sapiens

Met Ala Arg Ala Arg Gln Glu Gly Ser Ser Pro Glu Pro Val Glu Gly 1 10 15

Leu Ala Arg Asp Gly Pro Arg Pro Phe Pro Leu Gly Arg Leu Val Pro 20 25 30

Ser Ala Val Ser Cys Gly Leu Cys Glu Pro Gly Leu Ala Ala Ala Pro

Ala Ala Pro Thr Leu Leu Pro Ala Ala Tyr Leu Cys Ala Pro Thr Ala

Pro Pro Ala Val Thr Ala Ala Leu Gly Gly Ser Arg Trp Pro Gly Gly 65 70 75 80

Pro Arg Ser Arg Pro Arg Gly Pro Arg Pro Asp Gly Pro Gln Pro Ser 85 90 95

Leu Ser Leu Ala Glu Gln His Leu Glu Ser Pro Val Pro Ser Ala Pro $100 \ 105 \ 110$

Gly Ala Leu Ala Gly Gly Pro Thr Gln Ala Ala Pro Gly Val Arg Gly

Glu Glu Glu Gln Trp Ala Arg Glu Ile Gly Ala Gln Leu Arg Arg Met 130 140

Ala Asp Asp Leu Asn Ala Gln Tyr Glu Arg Arg Arg Gln Glu Gln 145 150 155 160

Gln Arg His Arg Pro Ser Pro Trp Arg Val Leu Tyr Asn Leu Ile Met
165 170 175

Gly Leu Leu Pro Leu Pro Arg Gly His Arg Ala Pro Glu Met Glu Pro 180 185 190

174 149 PRT

Homo sapiens

Met Pro Gly His Leu Gln Glu Gly Phe Gly Cys Val Val Thr Asn Arg 1 10 15

Phe Asp Gln Leu Phe Asp Asp Glu Ser Asp Pro Phe Glu Val Leu Lys

Ala Ala Glu Asn Lys Lys Glu Ala Gly Arg Gly Gly Val Gly Gly 35 45

Pro Gly Ala Lys Ser Ala Ala Gln Ala Ala Gln Thr Asn Ser Asn

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ala Ala Gly Lys Gln Leu Arg Lys Glu Ser Gln Lys Asp Arg Lys Asn 65 70 80 Pro Leu Pro Arg Ser Val Gly Val Val Asp Lys Lys Glu Glu Thr Gln
85 90 95 Pro Pro Val Ala Leu Lys Lys Glu Gly Ile Arg Arg Val Gly Arg Arg 100 105 110 Pro Asp Gln Gln Leu Gln Gly Glu Gly Lys Ile Ile Asp Arg Arg Pro 115 120 125Glu Arg Gln Pro Pro Cys Glu Arg Arg Phe Glu Lys Pro Leu Glu Glu 130 140

Lys Gly Glu Gly Gly

<210> 175 <211> 390 <212> PRT <213> Homo sapiens

Met Asn Ser Leu Ser Glu Ala Asn Thr Lys Phe Met Phe Asp Leu Phe 10 15Gln Gln Phe Arg Lys Ser Lys Glu Asn Asn Ile Phe Tyr Ser Pro Ile $20 \hspace{1cm} 25 \hspace{1cm} 30$ Ser Ile Thr Ser Ala Leu Gly Met Val Leu Leu Gly Ala Lys Asp Asn $35 \hspace{1cm} 40 \hspace{1cm} 45$ Thr Ala Gln Gln Ile Ser Lys Val Leu His Phe Asp Gln Val Thr Glu Asn Thr Thr Glu Lys Ala Ala Thr Tyr His Val Asp Arg Ser Gly Asn 65 70 75 80 Val His His Gln Phe Gln Lys Leu Leu Thr Glu Phe Asn Lys Ser Thr 85 90 95 Asp Ala Tyr Glu Leu Lys Ile Ala Asn Lys Leu Phe Gly Glu Lys Thr 100 105 110 Tyr Gln Phe Leu Gln Glu Tyr Leu Asp Ala Ile Lys Lys Phe Tyr Gln
115 120 125 Thr Ser Val Glu Ser Thr Asp Phe Ala Asn Ala Pro Glu Glu Ser Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Gln Thr Asn Glu Lys Ile Lys 145 150 155 160Asn Leu Phe Pro Asp Gly Thr Ile Gly Asn Asp Thr Thr Leu Val Leu 165 170 175 Val Asn Ala Ile Tyr Phe Lys Gly Gln Trp Glu Asn Lys Phe Lys Lys 180 185 190 Glu Asn Thr Lys Glu Glu Lys Phe Trp Pro Asn Lys Asn Thr Tyr Lys 195 200 205

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Ser Val Gln Met Met Arg Gln Tyr Asn Ser Phe Asn Phe Ala Leu Leu
210 215 220

Glu Asp Val Gln Ala Lys Val Leu Glu Ile Pro Tyr Lys Gly Lys Asp 225 230 235 240 Leu Ser Met Ile Val Leu Leu Pro Asn Glu Ile Asp Gly Leu Gln Lys 250 255 Leu Glu Glu Lys Leu Thr Ala Glu Lys Leu Met Glu Trp Thr Ser Leu 260 265 270 Gln Asn Met Arg Glu Thr Cys Val Asp Leu His Leu Pro Arg Phe Lys 275 280 285 Met Glu Glu Ser Tyr Asp Leu Lys Asp Thr Leu Arg Thr Met Gly Met Val Asn Ile Phe Asn Gly Asp Ala Asp Leu Ser Gly Met Thr Trp Ser His Gly Leu Ser Val Ser Lys Val Leu His Lys Ala Phe Val Glu Val Thr Glu Glu Gly Val Glu Ala Ala Ala Ala Thr Ala Val Val Val Val 340 345 Glu Leu Ser Ser Pro Ser Thr Asn Glu Glu Phe Cys Cys Asn His Pro 355 360 365Phe Leu Phe Phe Ile Arg Gln Asn Lys Thr Asn Ser Ile Leu Phe Tyr Gly Arg Phe Ser Ser Pro

176 541 PRT

Met Val Ala Asp Pro Pro Arg Asp Ser Lys Gly Leu Ala Ala Ala Glu Pro Thr Ala Asn Gly Gly Leu Ala Leu Ala Ser Ile Glu Asp Gln Gly 20 25 30 Ala Ala Gly Gly Tyr Cys Gly Ser Arg Asp Gln Val Arg Arg Cys 35 40 45 Leu Arg Ala Asn Leu Leu Val Leu Leu Thr Val Val Ala Val Val Ala 50 55 60 Gly Val Ala Leu Gly Leu Gly Val Ser Gly Ala Gly Gly Ala Leu Ala 65 70 75 80 Leu Gly Pro Glu Arg Leu Ser Ala Phe Val Phe Pro Gly Glu Leu Leu 85 90 95 Leu Arg Leu Leu Arg Met Ile Ile Leu Pro Leu Val Val Cys Ser Leu 100 105 110 Ile Gly Gly Ala Ala Ser Leu Asp Pro Gly Ala Leu Gly Arg Leu Gly 115 120 125



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Ala Trp Ala Leu Leu Phe Phe Leu Val Thr Thr Leu Leu Ala Ser Ala

130

135

140

Leu Gly Val Gly Leu Ala Leu Ala Leu Gln Pro Gly Ala Ala Ser Ala 145 150 160 Ala Ile Asn Ala Ser Val Gly Ala Ala Gly Ser Ala Glu Asn Ala Pro 165 170 175 Ser Lys Glu Val Leu Asp Ser Phe Leu Asp Leu Ala Arg Asn Ile Phe $180 \hspace{1cm} 185 \hspace{1cm} 190 \hspace{1cm}$ Pro Ser Asn Leu Val Ser Ala Ala Phe Arg Ser Tyr Ser Thr Thr Tyr 195 200 205 Glu Glu Arg Asn Ile Thr Gly Thr Arg Val Lys Val Pro Val Gly Gln 210 220 Glu Val Glu Gly Met Asn Ile Leu Gly Leu Val Val Phe Ala Ile Val 225 230 235 240 Phe Gly Val Ala Leu Arg Lys Leu Gly Pro Glu Gly Glu Leu Leu Ile 245 250 255 Arg Phe Phe Asn Ser Phe Asn Glu Ala Thr Met Val Leu Val Ser Trp 260 265 270 Ile Met Trp Tyr Ala Pro Val Gly Ile Met Phe Leu Val Ala Gly Lys 275 280 285 Ile Val Glu Met Glu Asp Val Gly Leu Leu Phe Ala Arg Leu Gly Lys 290 295 300 Tyr Ile Leu Cys Cys Leu Leu Gly His Ala Ile His Gly Leu Leu Val 305 310 315 320 Leu Pro Leu Ile Tyr Phe Leu Phe Thr Arg Lys Asn Pro Tyr Arg Phe 325 330 335 Leu Trp Gly Ile Val Thr Pro Leu Ala Thr Ala Phe Gly Thr Ser Ser 345 350 Ser Ser Ala Thr Leu Pro Leu Met Met Lys Cys Val Glu Glu Asn Asn 355 360 365 Gly Val Ala Lys His Ile Ser Arg Phe Ile Leu Pro Ile Gly Ala Thr 370 375 380 Val Asn Met Asp Gly Ala Ala Leu Phe Gln Cys Val Ala Ala Val Phe 385 390 395 400 Ile Ala Gln Leu Ser Gln Gln Ser Leu Asp Phe Val Lys Ile Ile Thr $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$ Ile Leu Val Thr Ala Thr Ala Ser Ser Val Gly Ala Ala Gly Ile Pro Ala Gly Gly Val Leu Thr Leu Ala Ile Ile Leu Glu Ala Val Asn Leu 435 440 445 Pro Val Asp His Ile Ser Leu Ile Leu Ala Val Asp Trp Leu Val Asp 450 450 460 Arg Ser Cys Thr Val Leu Asn Val Glu Gly Asp Ala Leu Gly Ala Gly

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 465 470 475 480 Leu Leu Gln Asn Tyr Val Asp Arg Thr Glu Ser Arg Ser Thr Glu Pro 485 490 495 Glu Leu Ile Gln Val Lys Ser Glu Leu Pro Leu Asp Pro Leu Pro Val 500 505 510 Pro Thr Glu Glu Gly Asn Pro Leu Leu Lys His Tyr Arg Gly Pro Ala 515 525

Gly Asp Ala Thr Val Ala Ser Glu Lys Glu Ser Val Met 530 540

<210> 177 <211> 482 <212> PRT <213> Homo sapiens

Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly $10 \ 15$

Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly 50 60

Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu 75 70 75

Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala 85 90 95

Gìn Ser Gìy Gìn Gìn Leu Gìu Trp Pro Gìu Ala Trp Arg Gìn Gìn Leu 100 105 110

Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val 115 120 125

Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser 130 140

Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser 150 150 155 Leu Glu Ser 160

Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu 165 170 175

Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val $180 \hspace{1cm} 185 \hspace{1cm} 190$

Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val 195 200 205

Asp Ser Leu Pro Leu Ile Thr Ala Ser Ile Leu Ser Lys Lys Leu Val 210 220

Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala 225 230 230 235

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Val Phe Pro Asn Gln Gln Ala Arg Glu Leu Ala Lys Thr Leu Val 245 250 255

Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala Leu Thr Ala 260 265 270 Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu Glu Val Glu 275 280 285 Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp Leu Arg Asp 290 295 300 Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser Gly His Ala Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala Leu Asp Asp 325 330 335 Gly Ser Ala Leu Gly Arg Phe Glu Arg Met Leu Ala Ala Gln Gly Val 340 345 350 Asp Pro Gly Leu Ala Arg Ala Leu Cys Ser Gly Ser Pro Ala Glu Arg 355 360 365Arg Gln Leu Leu Pro Arg Ala Arg Glu Gln Glu Leu Leu Ala Pro 370 375 380 Ala Asp Gly Thr Val Glu Leu Val Arg Ala Leu Pro Leu Ala Leu Val 385 390 395 400 Leu His Glu Leu Gly Ala Gly Arg Ser Arg Ala Gly Glu Pro Leu Arg 410 415 Leu Gly Val Gly Ala Glu Leu Leu Val Asp Val Gly Gln Arg Leu Arg 420 425 430 Arg Gly Thr Pro Trp Leu Arg Val His Arg Asp Gly Pro Ala Leu Ser 435 440 Gly Pro Gln Ser Arg Ala Leu Gln Glu Ala Leu Val Leu Ser Asp Arg 450 455 460 Ala Pro Phe Ala Ala Pro Leu Pro Phe Ala Glu Leu Val Leu Pro Pro 465 470 475

<210> 178
<211> 399

Gln Gln

<212> PRT <213> Homo sapiens

<400> 178

Met Tyr Ser Pro Arg Gly Ser Gln Gly Arg Gly Thr Ala Glu Ala Thr 1 5 10 15

Ala Asn Ser Pro Ser Pro Pro Ile Ala Pro Ser His Ser Arg Val Thr

Phe Ser Leu Ser Thr Leu His Thr Leu Ser Pro Pro Arg Pro Phe 35 40 45

Pro Ser Val Ser Arg Ala Ala Ala Gln Lys Pro His His Leu His Pro 50 60

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

His Ile Leu Leu Ala Gly Ser Ala Ala Val Pro Pro Arg Val Leu Lys

75 80

Ala Glu Met Asn Asn Thr Ala Ala Ser Pro Met Ser Thr Ala Thr Ser

Ala Glu Met Asn Asn Thr Ala Ala Ser Pro Met Ser Thr Ala Thr Ser 90 95 Ser Ser Gly Arg Ser Thr Gly Lys Ser Ile Ser Phe Ala Thr Glu Leu $100 \hspace{0.25cm} 105 \hspace{0.25cm} 110$ Gln Ser Met Met Tyr Ser Leu Gly Asp Ala Arg Arg Pro Leu His Glu 115 120 126 Thr Ala Val Leu Val Glu Asp Val Val His Thr Gln Leu Ile Asn Leu 130 135 140 Leu Gln Gln Ala Ala Glu Val Ser Gln Leu Arg Gly Ala Arg Val Ile 145 155 160 Thr Pro Glu Asp Leu Leu Phe Leu Met Arg Lys Asp Lys Lys Leu 165 170 175 Arg Arg Leu Leu Lys Tyr Met Phe Ile Arg Asp Tyr Lys Ser Lys Ile 180 185 190 Val Lys Gly Ile Asp Glu Asp Asp Leu Leu Glu Asp Lys Leu Ser Gly 195 200 205 Ser Asn Asn Ala Asn Lys Arg Gln Lys Ile Ala Gln Asp Phe Leu Asn 210 220 Ser Ile Asp Gln Thr Gly Glu Leu Leu Ala Met Phe Glu Asp Asp Glu 225 230 235 240 Ile Asp Glu Val Lys Gln Glu Arg Met Glu Arg Ala Glu Arg Gln Thr $245 \hspace{0.25cm} 250 \hspace{0.25cm} 255$ Arg Ile Met Asp Ser Ala Gln Tyr Ala Glu Phe Cys Glu Ser Arg Gln 260 265 270Leu Ser Phe Ser Lys Lys Ala Ser Lys Phe Arg Asp Trp Leu Asp Cys 275 285 Ser Ser Met Glu Ile Lys Pro Asn Val Val Ala Met Glu Ile Leu Ala 290 300 Tyr Leu Ala Tyr Glu Thr Val Ala Gln Leu Val Asp Leu Ala Leu Leu 305 310 315 Val Arg Gln Asp Met Val Thr Lys Ala Gly Asp Pro Phe Ser His Ala 325 330 335 Ile Ser Ala Thr Phe Ile Gln Tyr His Asn Ser Ala Glu Ser Thr Ala $340 \hspace{1.5cm} 345$ Ala Cys Gly Val Glu Ala His Ser Asp Ala Ile Gln Pro Cys His Ile 355 360 365 Arg Glu Ala Ile Arg Arg Tyr Ser His Arg Ile Gly Pro Leu Ser Pro Phe Thr Asn Ala Tyr Arg Arg Asn Gly Met Ala Phe Leu Ala Cys 385

<210> 179

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Homo sapiens

<400> 179 Met Ala Ala Leu Arg Tyr Ala Gly Leu Asp Asp Thr Asp Ser Glu Asp 1 10 15 Glu Leu Pro Pro Gly Trp Glu Glu Arg Thr Thr Lys Asp Gly Trp Val Tyr Tyr Ala Asn His Thr Glu Glu Lys Thr Gln Trp Glu His Pro Lys 35 40 45Thr Gly Lys Arg Lys Arg Val Ala Gly Asp Leu Pro Tyr Gly Trp Glu 50 60 Gln Glu Thr Asp Glu Asn Gly Gln Val Phe Phe Val Asp His Ile Asn 65 70 75 80 Asn Pro Thr Lys Pro Thr Thr Arg Gln Arg Tyr Asp Gly Ser Thr Thr $100 \hspace{1cm} 105 \hspace{1cm} 110$ Ala Met Glu Ile Leu Gln Gly Arg Asp Phe Thr Gly Lys Val Val 115 120 125 Val Thr Gly Ala Asn Ser Gly Ile Gly Phe Glu Thr Ala Lys Ser Phe 130 135 Ala Leu His Gly Ala His Val Ile Leu Ala Cys Arg Asn Met Ala Arg 145 150 155 160Ala Ser Glu Ala Val Ser Arg Ile Leu Glu Glu Trp His Lys Ala Lys 165 170 175 Val Glu Ala Met Thr Leu Asp Leu Ala Leu Leu Arg Ser Val Gln His 180 185 190 Phe Ala Glu Ala Phe Lys Ala Lys Asn Val Pro Leu His Val Leu Val Cys Asn Ala Ala Thr Phe Ala Leu Pro Trp Ser Leu Thr Lys Asp Gly 210 215 Leu Glu Thr Thr Phe Gln Val Asn His Leu Gly His Phe Tyr Leu Val 225 230 235Gln Leu Leu Gln Asp Val Leu Cys Arg Ser Ala Pro Ala Arg Val Ile 245 250 255 Val Val Ser Ser Glu Ser His Arg Phe Thr Asp Ile Asn Asp Ser Leu 260 265 270 Gly Lys Leu Asp Phe Ser Arg Leu Ser Pro Thr Lys Asn Asp Tyr Trp 275 280 285 Ala Met Leu Ala Tyr Asn Arg Ser Lys Leu Cys Asn Ile Leu Phe Ser 290 300Asn Glu Leu His Arg Arg Leu Ser Pro Arg Gly Val Thr Ser Asn Ala

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Val His Pro Gly Asn Met Met Tyr Ser Asn Ile His Arg Ser Trp Trp 325 330 335

Val Tyr Thr Leu Leu Phe Thr Leu Ala Arg Pro Phe Thr Lys Ser Met Gln Gln Gly Ala Ala Thr Thr Val Tyr Cys Ala Ala Val Pro Glu Leu 355 360 365 Glu Gly Leu Gly Gly Met Tyr Phe Asn Asn Cys Cys Arg Cys Met Pro Ser Pro Glu Ala Gln Ser Glu Glu Thr Ala Arg Thr Leu Trp Ala Leu 385 390 395 400 Ser Glu Arg Leu Ile Gln Glu Arg Leu Gly Ser Gln Ser Gly

180 295 PRT Homo sapiens Met Val Pro Val Leu Leu Ser Leu Leu Leu Leu Gly Pro Ala Val Pro Gln Glu Asn Gln Asp Gly Arg Tyr Ser Leu Thr Tyr Ile Tyr Thr Gly Leu Ser Lys His Val Glu Asp Val Pro Ala Phe Gln Ala Leu Gly 35 40 45 Ser Leu Asn Asp Leu Gln Phe Phe Arg Tyr Asn Ser Lys Asp Arg Lys 50 60 Ser Gln Pro Met Gly Leu Trp Arg Gln Val Glu Gly Met Glu Asp Trp 65 70 75 80 Lys Gln Asp Ser Gln Leu Gln Lys Ala Arg Glu Asp Ile Phe Met Glu 85 90 95 Thr Leu Lys Asp Ile Val Glu Tyr Tyr Asn Asp Ser Asn Gly Ser His $100 \hspace{1cm} 105 \hspace{1cm} 110$

Val Leu Gln Gly Arg Phe Gly Cys Glu Ile Glu Asn Asn Arg Ser Ser 115 120 125 Gly Ala Phe Trp Lys Tyr Tyr Asp Gly Lys Asp Tyr Ile Glu Phe Asn Lys Glu Ile Pro Ala Trp Val Pro Phe Asp Pro Ala Ala Gln Ile Thr Lys Gln Lys Trp Glu Ala Glu Pro Val Tyr Val Gln Arg Ala Lys 165 170 175Ala Tyr Leu Glu Glu Glu Cys Pro Ala Thr Leu Arg Lys Tyr Leu Lys 180 185 190

Thr Ser His Gln Ala Pro Gly Glu Lys Lys Lys Leu Lys Cys Leu Ala 210 220

Tyr Ser Lys Asn Ile Leu Asp Arg Gln Asp Pro Pro Ser Val Val Val 195 200 205

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Tyr Asp Phe Tyr Pro Gly Lys Ile Asp Val His Trp Thr Arg Ala Gly Glu Val Gln Glu Pro Glu Leu Arg Gly Asp Val Leu His Asn Gly Asn 245 250 255 Gly Thr Tyr Gln Ser Trp Val Val Val Ala Val Pro Pro Gln Asp Thr Ala Pro Tyr Ser Cys His Val Gln His Ser Ser Leu Ala Gln Pro Leu 275 280 285 Val Val Pro Trp Glu Ala Ser

<210> 181 <211> 507 <212> PRT <213> Homo sapiens

Met Ala Gly Ala Gly Pro Lys Arg Arg Ala Leu Ala Ala Pro Ala Ala 1 10 15 Glu Glu Lys Glu Glu Ala Arg Glu Lys Met Leu Ala Ala Lys Ser Ala 20 25 30 Asp Gly Ser Ala Pro Ala Gly Glu Gly Glu Gly Val Thr Leu Gln Arg 40 45Asn Ile Thr Leu Leu Asn Gly Val Ala Ile Ile Val Gly Thr Ile Ile 50 60 Gly Ser Gly Ile Phe Val Thr Pro Thr Gly Val Leu Lys Glu Ala Gly 65 70 75 80 Ser Pro Gly Leu Ala Leu Val Val Trp Ala Ala Cys Gly Val Phe Ser 85 90 95 Ile Val Gly Ala Leu Cys Tyr Ala Glu Leu Gly Thr Thr Ile Ser Lys 100 105 110 Ser Gly Gly Asp Tyr Ala Tyr Met Leu Glu Val Tyr Gly Ser Leu Pro 115 120 125 Ala Phe Leu Lys Leu Trp Ile Glu Leu Leu Ile Ile Arg Pro Ser Ser 130 135 140 Gln Tyr Ile Val Ala Leu Val Phe Ala Thr Tyr Leu Leu Lys Pro Leu 145 150 160 Phe Pro Thr Cys Pro Val Pro Glu Glu Ala Ala Lys Leu Val Ala Cys 165 170 175 Leu Cys Val Leu Leu Thr Ala Val Asn Cys Tyr Ser Val Lys Ala 180 185 190 Ala Thr Arg Val Gln Asp Ala Phe Ala Ala Ala Lys Leu Leu Ala Leu 195 200 205 Ala Leu Ile Ile Leu Leu Gly Phe Val Gln Ile Gly Lys Gly Asp Val 210 220 Ser Asn Leu Asp Pro Asn Phe Ser Phe Glu Gly Thr Lys Leu Asp Val



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gly ASM Ile Val Leu Ala Leu Tyr Ser Gly Leu Phe Ala Tyr Gly Gly Trp Asn Tyr Leu Asn Phe Val Thr Glu Glu Met Ile Asn Pro Tyr Arg Asn Leu Pro Leu Ala Ile Ile Ile Ser Leu Pro Ile Val Thr Leu Val 275 280 285 Tyr Val Leu Thr Asn Leu Ala Tyr Phe Thr Thr Leu Ser Thr Glu Gln 290 295 300 Met Leu Ser Ser Glu Ala Val Ala Val Asp Phe Gly Asn Tyr His Leu 305 310 315 320 Gly Val Met Ser Trp Ile Ile Pro Val Phe Val Gly Leu Ser Cys Phe 325 Phe 330Gly Ser Val Asn Gly Ser Leu Phe Thr Ser Ser Arg Leu Phe Phe Val Gly Ser Arg Glu Gly His Leu Pro Ser Ile Leu Ser Met Ile His Pro 355 360 365Gln Leu Leu Thr Pro Val Pro Ser Leu Val Phe Thr Cys Val Met Thr 370 380 Leu Leu Tyr Ala Phe Ser Lys Asp Ile Phe Ser Val Ile Asn Phe Phe 385 390 395 400 Ser Phe Phe Asn Trp Leu Cys Val Ala Leu Ala Ile Ile Gly Met Ile 405 410 415 Trp Leu Arg His Arg Lys Pro Glu Leu Glu Arg Pro Ile Lys Val Asn 420 425 430 Leu Ala Leu Pro Val Phe Phe Ile Leu Ala Cys Leu Phe Leu Ile Ala 435 440 445 Ile Leu Ser Gly Leu Pro Val Tyr Phe Phe Gly Val Trp Trp Lys Asn 465 470 475 480 Lys Pro Lys Trp Leu Leu Gln Gly Ile Phe Ser Thr Thr Val Leu Cys $485 \hspace{1.5cm} 490 \hspace{1.5cm} \cdot \hspace{1.5cm} 195 \hspace{1.$ Gln Lys Leu Met Gln Val Val Pro Gln Glu Thr <210> 182 <211> 1210 <212> PRT <213> Homo sapiens

Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala 1 10 15

Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln 20 25 30

Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn 50 60 Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val $85 \hspace{1cm} 90 \hspace{1cm} 95$ Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr 100 105 110 Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu 130 140 His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu 145 155 160 Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met 165 170 175 Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro 180 185 190 Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln 195 200 205 Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg 210 225 220 Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys 225 230 235 240 Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp 245 250 255 Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro 260 265 270 Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly 275 280 285 Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His 290 295 300Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu 305 310 315 Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn 345 350 Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp 355 360 365 Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu 385 390 395 400 Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp 405 410 415Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln 420 425 His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu 435 440 445 Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser 450 460 Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu 465 470 475 480 Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu 485 490 495Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro 500 505 Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn 515 525 Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Lys Leu Leu Glu Gly 530 540 Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro 545 550 555 560 Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro 575 Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val 580 585 Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp 595 600 605 Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys 610 620 Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly 625 630 635 Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu 655 Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg His $660 \hspace{0.25cm} 665$ Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu 675 680 685 Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu 690 695 700 Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser 705 710 715 720 Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.st25.txt Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser 755 760 765 Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp 785 790 800 Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn 815 Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg 820 825 830 Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro 835 840 845 Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala 850 855 Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp 865 870 875 880 Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp 885 890 895 Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu 915 920 925 Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr 930 935 940 Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys 945 950 955 960 Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln $965 \hspace{0.5cm} 970 \hspace{0.5cm} 975$ Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro 980 985 990 Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp 995 1000 1005Asp Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu 1025 1030 1035 Ser Ala Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn 1040 1050Gly Leu Gln Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg 1055 1060 1065

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protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Tyr Ser Ser Asp Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp 1070 1080

Asp Thr Phe Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro

Lys Arg Pro Ala Gly Ser Val Gln Asn Pro Val Tyr His Asn Gln 1100 1110

Pro Leu Asn Pro Ala Pro Ser Arg Asp Pro His Tyr Gln Asp Pro 1115 Gln Asp Pro

His Ser Thr Ala Val Gly Asn Pro Glu Tyr Leu Asn Thr Val Gln 1130 1140

Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala His Trp Ala 1145 1155

Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Tyr Gln 1160 1170

Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys 1175 1180

Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln 1190 1200

Ser Ser Glu Phe Ile Gly Ala

<210> 183 <211> 1371 <212> PRT <213> Homo sapiens

<400> 183

Met Thr Thr Lys Arg Ser Leu Phe Val Arg Leu Val Pro Cys Arg Cys 10 15

Leu Arg Gly Glu Glu Thr Val Thr Thr Leu Asp Tyr Ser His Cys 20 25 30

Ser Leu Glu Gln Val Pro Lys Glu Ile Phe Thr Phe Glu Lys Thr Leu $35 \hspace{1cm} 40 \hspace{1cm} 45$

Glu Glu Leu Tyr Leu Asp Ala Asn Gln Ile Glu Glu Leu Pro Lys Gln 50 60

Leu Phe Asn Cys Gln Ser Leu His Lys Leu Ser Leu Pro Asp Asn Asp 65 70 75 80

Leu Thr Thr Leu Pro Ala Ser Ile Ala Asn Leu Ile Asn Leu Arg Glu 85 90 95

Leu Asp Val Ser Lys Asm Gly Ile Glm Glu Phe Pro Glu Asm Ile Lys 100 105 110

Asn Cys Lys Val Leu Thr Ile Val Glu Ala Ser Val Asn Pro Ile Ser 115 120 125

Lys Leu Pro Asp Gly Phe Ser Gln Leu Leu Asn Leu Thr Gln Leu Tyr 130 140

Leu Asn Asp Ala Phe Leu Glu Phe Leu Pro Ala Asn Phe Gly Arg Leu 145 150 160



protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Lys Leu Gln Ile Leu Glu Leu Arg Glu Asn Gln Leu Lys Met Leu 165 170 175 Pro Lys Thr Met Asn Arg Leu Thr Gln Leu Glu Arg Leu Asp Leu Gly 185 190 Ser Asn Glu Phe Thr Glu Val Pro Glu Val Leu Glu Gln Leu Ser Gly 195 200 205 Leu Lys Glu Phe Trp Met Asp Ala Asn Arg Leu Thr Phe Ile Pro Gly 210 220 Phe Ile Gly Ser Leu Lys Gln Leu Thr Tyr Leu Asp Val Ser Lys Asn 225 230 235 240 Asn Ile Glu Met Val Glu Glu Gly Ile Ser Thr Cys Glu Asn Leu Gln 245 250 Asp Leu Leu Ser Ser Asn Ser Leu Gln Gln Leu Pro Glu Thr Ile $\frac{260}{260}$ Gly Ser Leu Lys Asn Ile Thr Thr Leu Lys Ile Asp Glu Asn Gln Leu 275 280 285 Met Tyr Leu Pro Asp Ser Ile Gly Gly Leu Ile Ser Val Glu Glu Leu 290 295 300 Asp Cys Ser Phe Asn Glu Val Glu Ala Leu Pro Ser Ser Ile Gly Gln 305 310 315 320 Leu Thr Asn Leu Arg Thr Phe Ala Ala Asp His Asn Tyr Leu Gln Gln 325 330 335Leu Pro Pro Glu Ile Gly Ser Trp Lys Asn Ile Thr Val Leu Phe Leu 340 345 His Ser Asn Lys Leu Glu Thr Leu Pro Glu Glu Met Gly Asp Met Gln 355 360 365 Lys Leu Lys Val Ile Asn Leu Ser Asp Asn Arg Leu Lys Asn Leu Pro $\frac{370}{370}$ Phe Ser Phe Thr Lys Leu Gln Gln Leu Thr Ala Met Trp Leu Ser Asp 385 390 395 400 Asn Gln Ser Lys Pro Leu Ile Pro Leu Gln Lys Glu Thr Asp Ser Glu 405 410 415 Thr Gln Lys Met Val Leu Thr Asn Tyr Met Phe Pro Gln Gln Pro Arg 420 425 430 Thr Glu Asp Val Met Phe Ile Ser Asp Asn Glu Ser Phe Asn Pro Ser 435 445 Leu Trp Glu Glu Gln Arg Lys Gln Arg Ala Gln Val Ala Phe Glu Cys 450 460 Asp Glu Asp Lys Asp Glu Arg Glu Ala Pro Pro Arg Glu Gly Asn Leu 465 470 475 Lys Arg Tyr Pro Thr Pro Tyr Pro Asp Glu Leu Lys Asn Met Val Lys 485 490 495



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Thr Val Gln Thr Ile Val His Arg Leu Lys Asp Glu Glu Thr Asn Glu
500 505 510

Asp Ser Gly Arg Asp Leu Lys Pro His Glu Asp Gln Gln Asp Ile Asn 515 525 Lys Asp val Gly Val Lys Thr Ser Glu Ser Thr Thr Thr Val Lys Ser 530 540 Lys Val Asp Glu Arg Glu Lys Tyr Met Ile Gly Asn Ser Val Gln Lys 545 550 555 Ile Ser Glu Pro Glu Ala Glu Ile Ser Pro Gly Ser Leu Pro Val Thr 565 570 575 Ala Asn Met Lys Ala Ser Glu Asn Leu Lys His Ile Val Asn His Asp 580 590 Asp Val Phe Glu Glu Ser Glu Glu Leu Ser Ser Asp Glu Glu Met Lys 595 600 605 Met Ala Glu Met Arg Pro Pro Leu Ile Glu Thr Ser Ile Asn Gln Pro Lys val val Ala Leu Ser Asn Asn Lys Lys Asp Asp Thr Lys Glu Thr 625 630 635 640 Asp Ser Leu Ser Asp Glu Val Thr His Asn Ser Asn Gln Asn Asn Ser 655 Asn Cys Ser Ser Pro Ser Arg Met Ser Asp Ser Val Ser Leu Asn Thr 660 670Asp Ser Ser Gln Asp Thr Ser Leu Cys Ser Pro Val Lys Gln Thr His 675 680 685 Ile Asp Ile Asn Ser Lys Ile Arg Gln Glu Asp Glu Asn Phe Asn Ser 690 700 Leu Leu Gln Asn Gly Asp Ile Leu Asn Ser Ser Thr Glu Glu Lys Phe Lys Ala His Asp Lys Lys Asp Phe Asn Leu Pro Glu Tyr Asp Leu Asn 725 735 Val Glu Glu Arg Leu Val Leu Ile Glu Lys Ser Val Asp Ser Thr Ala 740 745 750 Thr Ala Asp Asp Thr His Lys Leu Asp His Ile Asn Met Asn Leu Asn 765 760 765 Lys Leu Ile Thr Asn Asp Thr Phe Gln Pro Glu Ile Met Glu Arg Ser Lys Thr Gln Asp Ile val Leu Gly Thr Ser Phe Leu Ser Ile Asn Ser Lys Glu Glu Thr Glu His Leu Glu Asn Gly Asn Lys Tyr Pro Asn Leu 805 810 815 Glu Ser Val Asn Lys Val Asn Gly His Ser Glu Glu Thr Ser Gln Ser 820 825 830 Pro Asn Arg Thr Glu Pro His Asp Ser Asp Cys Ser Val Asp Leu Gly



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Ser Lys Ser Thr Glu Asp Leu Ser Pro Gln Lys Ser Gly Pro Val Gly Ser Val Val Lys Ser His Ser Ile Thr Asn Met Glu Ile Gly Gly 865 870 875 Leu Lys Ile Tyr Asp Ile Leu Ser Asp Asn Gly Pro Gln Gln Pro Ser 885 890 895 Thr Thr Val Lys Ile Thr Ser Ala Val Asp Gly Lys Asn Ile Val Arg Ser Lys Ser Ala Thr Leu Leu Tyr Asp Gln Pro Leu Gln Val Phe Thr 915 920 925 Gly Ser Ser Ser Ser Asp Leu Ile Ser Gly Thr Lys Ala Ile Phe Lys Phe Asp Ser Asn His Asn Pro Glu Glu Pro Asn Ile Ile Arg Gly 945 950 955 960 Pro Thr Ser Gly Pro Gln Ser Ala Pro Gln Ile Tyr Gly Pro Pro Gln 975 Tyr Asn Ile Gln Tyr Ser Ser Ser Ala Ala Val Lys Asp Thr Leu Trp $980 \hspace{1.5cm} 985 \hspace{1.5cm} 990$ His Ser Lys Gln Asn Pro Gln Ile Asp His Ala Ser Phe Pro Pro Gln 995 1000 Leu Leu Pro Arg Ser Glu Ser Thr Glu Asn Gln Ser Tyr Ala Lys 1010 1020 His Ser Ala Asn Met Asn Phe Ser Asn His Asn Asn Val Arg Ala Asn Thr Ala Tyr His Leu His Gln Arg Leu Gly Pro Ala Arg His 1040 1045 1050 Gly Glu Met Trp Ala Ile Ser Pro Asn Asp Arg Leu Ile Pro Ala 1055 1060 1065 Val Thr Arg Ser Thr Ile Gln Arg Gln Ser Ser Val Ser Ser Thr 1070 1075 1080Ala Ser Val Asn Leu Gly Asp Pro Gly Ser Thr Arg Arg Ala Gln Ile Pro Glu Gly Asp Tyr Leu Ser Tyr Arg Glu Phe His Ser Ala 1100 1105 1110Gly Arg Thr Pro Pro Met Met Pro Gly Ser Gln Arg Pro Leu Ser 1115 1120 1125 Ala Arg Thr Tyr Ser Ile Asp Gly Pro Asn Ala Ser Arg Pro Gln Ser Ala Arg Pro Ser Ile Asn Glu Ile Pro Glu Arg Thr Met Ser Val Ser Asp Phe Asn Tyr Ser Arg Thr Ser Pro Ser Lys Arg Pro 1160 1170

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Asn Ala Arg Val Gly Ser Glu His Ser Leu Leu Asp Pro Pro Gly
1175 1180 1185

Lys Ser Lys Val Pro Arg Asp Trp Arg Glu Gln Val Leu Arg His 1190 1195 1200

Ile Glu Ala Lys Lys Leu Glu Lys Met Pro Leu Ser Asn Gly Gln
1205 1210 1215

Met Gly Gln Pro Leu Arg Pro Gln Ala Asn Tyr Ser Gln Ile His

His Pro Pro Gln Ala Ser Val Ala Arg His Pro Ser Arg Glu Gln 1235 1240 1245

Leu Ile Asp Tyr Leu Met Leu Lys Val Ala His Gln Pro Pro Tyr 1250 1260

Thr Gln Pro His Cys Ser Pro Arg Gln Gly His Glu Leu Ala Lys 1265 1270 1275

Gln Glu Ile Arg Val Arg Val Glu Lys Asp Pro Glu Leu Gly Phe 1280 1285 1290

Ser Ile Ser Gly Gly Val Gly Gly Arg Gly Asn Pro Phe Arg Pro

Asp Asp Gly Ile Phe Val Thr Arg Val Gln Pro Glu Gly Pro 1310 1320

Ala Ser Lys Leu Leu G^ln Pro Gly Asp Lys Ile Ile Gln Ala Asn 1325 1330 1335

Gly Tyr Ser Phe Ile Asn Ile Glu His Gly Gln Ala Val Ser Leu 1340 1350

Leu Lys Thr Phe Gln Asn Thr Val Glu Leu Ile Ile Val Arg Glu 1355 1360 1365

Val Ser Ser 1370

<210> 184 <211> 581 <212> PRT <213> Homo sapiens

Met Ala Val Glu Asp Glu Gly Leu Arg Val Phe Gln Ser Val Lys Ile 1 10 15

Lys Ile Gly Glu Ala Lys Asn Leu Pro Ser Tyr Pro Gly Pro Ser Lys 20 30

Met Arg Asp Cys Tyr Cys Thr Val Asn Leu Asp Gln Glu Glu Val Phe

Arg Thr Lys Ile Val Glu Lys Ser Leu Cys Pro Phe Tyr Gly Glu Asp

Phe Tyr Cys Glu Ile Pro Arg Ser Phe Arg His Leu Ser Phe Tyr Ile

Phe Asp Arg Asp Val Phe Arg Arg Asp Ser Ile Ile Gly Lys Val Ala



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Gln Lys Glu Asp Leu Gln Lys Tyr His Asn Arg Asp Thr Trp Phe 100 105 110 Gln Leu Gln His Val Asp Ala Asp Ser Glu Val Gln Gly Lys Val His Leu Glu Leu Arg Leu Ser Glu Val Ile Thr Asp Thr Gly Val Val Cys 130 135 140 His Lys Leu Ala Thr Arg Ile Val Glu Cys Gln Gly Leu Pro Ile Val 145 150 155 160 Asn Gly Gln Cys Asp Pro Tyr Ala Thr Val Thr Leu Ala Gly Pro Phe
165 170 175 Arg Ser Glu Ala Lys Lys Thr Lys Val Lys Arg Lys Thr Asn Asn Pro $180 \hspace{1cm} 185 \hspace{1cm} 190 \hspace{1cm}$ Gln Phe Asp Glu Val Phe Tyr Phe Glu Val Thr Arg Pro Cys Ser Tyr 195 200 205 Ser Lys Lys Ser His Phe Asp Phe Glu Glu Glu Asp Val Asp Lys Leu Glu Ile Arg Val Asp Leu Trp Asn Ala Ser Asn Leu Lys Phe Gly Asp 225 230 235 Glu Phe Leu Gly Glu Leu Arg Ile Pro Leu Lys Val Leu Arg Gln Ser 245 250 255Ser Ser Tyr Glu Ala Trp Tyr Phe Leu Gln Pro Arg Asp Asn Gly Ser 260 265 270 Lys Ser Leu Lys Pro Asp Asp Leu Gly Ser Leu Arg Leu Asn Val Val 275 280 Tyr Thr Glu Asp His Val Phe Ser Ser Asp Tyr Tyr Ser Pro Leu Arg 290 295 300 Asp Leu Leu Leu Lys Ser Ala Asp Val Glu Pro Val Ser Ala Ser Ala 305 310 315 Ala His Ile Leu Gly Glu Val Cys Arg Glu Lys Gln Glu Ala Ala Val . 325 330 335 Pro Leu Val Arg Leu Phe Leu His Tyr Gly Arg Val Val Pro Phe Ile 345 350 Ser Ala Ile Ala Ser Ala Glu Val Lys Arg Thr Gln Asp Pro Asn Thr 355 360 365 Ile Phe Arg Gly Asn Ser Leu Ala Ser Lys Cys Ile Asp Glu Thr Met
370 375 380 Lys Leu Ala Gly Met His Tyr Leu His Val Thr Leu Lys Pro Ala Ile 385 390 395 400Glu Glu Ile Cys Gln Ser His Lys Pro Cys Glu Ile Asp Pro Val Lys 405 410 415 Leu Lys Asp Gly Glu Asn Leu Glu Asn Asn Met Glu Asn Leu Arg Gln 420 425 430 Tyr Val Asp Arg Val Phe His Ala Ile Thr Glu Ser Gly Val Ser Cys

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 435 440 445

Pro Thr Val Met Cys Asp Ile Phe Phe Ser Leu Arg Glu Ala Ala Ala 450 455 460 Lys Arg Phe Gln Asp Asp Pro Asp Val Arg Tyr Thr Ala Val Ser Ser 465 470 475 480 Phe Ile Phe Leu Arg Phe Phe Ala Pro Ala Ile Leu Ser Pro Asn Leu
485 490 495 Phe Gln Leu Thr Pro His His Thr Asp Pro Gln Thr Ser Arg Thr Leu 500 505 Thr Leu Ile Ser Lys Thr Val Gln Thr Leu Gly Ser Leu Ser Lys Ser Lys Ser Ala Ser Phe Lys Glu Ser Tyr Met Ala Thr Phe Tyr Glu Phe 530 540Phe Asn Glu Gln Lys Tyr Ala Asp Ala Val Lys Asn Phe Leu Asp Leu 545 550 555 560 Ile Ser Ser Ser Gly Arg Arg Asp Pro Lys Ser Val Glu Gln Pro Ile 565 570 575 Val Leu Lys Glu Gly

<210> 185 <211> 532 <212> PRT <213> Homo sapiens

Met Glu Leu Asp Leu Ser Pro Pro His Leu Ser Ser Ser Pro Glu Asp 1 10 15 Leu Cys Pro Ala Pro Gly Thr Pro Pro Gly Thr Pro Arg Pro Pro Asp $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$ Thr Pro Leu Pro Glu Glu Val Lys Arg Ser Gln Pro Leu Leu Ile Pro Thr Thr Gly Arg Lys Leu Arg Glu Glu Glu Arg Arg Ala Thr Ser Leu 50 60 Pro Ser Ile Pro Asn Pro Phe Pro Glu Leu Cys Ser Pro Pro Ser Gln 65 70 75 80 Ser Pro Ile Leu Gly Gly Pro Ser Ser Ala Arg Gly Leu Leu Pro Arg Asp Ala Ser Arg Pro His Val Val Lys Val Tyr Ser Glu Asp Gly Ala

Cys Arg Ser Val Glu Val Ala Ala Gly Ala Thr Ala Arg His Val Cys 115 120 125

Glu Met Leu Val Gln Arg Ala His Ala Leu Ser Asp Glu Thr Trp Gly 130 140

Leu Val Glu Cys His Pro His Leu Ala Leu Glu Arg Gly Leu Glu Asp 145 150 155 160



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
His Glu Ser Val Val Glu Val Gln Ala Ala Trp Pro Val Gly Gly Asp
165
170
175

Ser Arg Phe Val Phe Arg Lys Asn Phe Ala Lys Tyr Glu Leu Phe Lys 180 185 . 190 Ser Ser Pro His Ser Leu Phe Pro Glu Lys Met Val Ser Ser Cys Leu 195 200 205 Asp Ala His Thr Gly Ile Ser His Glu Asp Leu Ile Gln Asn Phe Leu 210 215 220 Asn Ala Gly Ser Phe Pro Glu Ile Gln Gly Phe Leu Gln Leu Arg Gly 225 230 235 Ser Gly Arg Lys Leu Trp Lys Arg Phe Phe Cys Phe Leu Arg Arg Ser 250 255 Gly Leu Tyr Tyr Ser Thr Lys Gly Thr Ser Lys Asp Pro Arg His Leu 260 265 270 Gln Tyr Val Ala Asp Val Asn Glu Ser Asn Val Tyr Val Val Thr Gln 275 280 285 Gly Arg Lys Leu Tyr Gly Met Pro Thr Asp Phe Gly Phe Cys Val Lys 290 295 300 Pro Asn Lys Leu Arg Asn Gly His Lys Gly Leu Arg Ile Phe Cys Ser 305 310 315 Glu Asp Glu Gln Ser Arg Thr Cys Trp Leu Ala Ala Phe Arg Leu Phe 325 $$ 330 $$ 335 Lys Tyr Gly Val Gln Leu Tyr Lys Asn Tyr Gln Gln Ala Gln Ser Arg 340 345His Leu His Pro Ser Cys Leu Gly Ser Pro Pro Leu Arg Ser Ala Ser Asp Asn Thr Leu Val Ala Met Asp Phe Ser Gly His Ala Gly Arg Val 370 380 ile Glu Asn Pro Arg Glu Ala Leu Ser Val Ala Leu Glu Glu Ala Gln 385 390 395 400 Ala Trp Arg Lys Lys Thr Asn His Arg Leu Ser Leu Pro Met Pro Ala 405 410 415 Ser Gly Thr Ser Leu Ser Ala Ala Ile His Arg Thr Gln Leu Trp Phe 420 425 430 His Gly Arg Ile Ser Arg Glu Glu Ser Gln Arg Leu Ile Gly Gln Gln 435 440 445 Gly Leu Val Asp Gly Leu Phe Leu Val Arg Glu Ser Gln Arg Asn Pro Gln Gly Phe Val Leu Ser Leu Cys His Leu Gln Lys Val Lys His Tyr 465 470 475 480 Leu Ile Leu Pro Ser Glu Glu Glu Gly Arg Leu Tyr Phe Ser Met Asp 485 490 495 Asp Gly Gln Thr Arg Phe Thr Asp Leu Leu Gln Leu Val Glu Phe His 500 505



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Gln Leu Asn Arg Gly Ile Leu Pro Cys Leu Leu Arg His Cys Cys Thr

Arg Val Ala Leu 530

<210> 186 <211> 1342 <212> PRT <213> Homo sapiens

<400> 186 Met Arg Ala Asn Asp Ala Leu Gln Val Leu Gly Leu Leu Phe Ser Leu $10 \ 15$ Ala Arg Gly Ser Glu Val Gly Asn Ser Gln Ala Val Cys Pro Gly Thr Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Glu Asn Gln Tyr Gln Thr 35 40 45Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu 50 55 60 Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile 65 70 75 80 Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95$ Leu Pro Leu Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp 100 105 110 Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser 115 125 125His Ala Leu Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser 130 135 140 Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr 145 150 160Ile Asp Trp Arg Asp Ile Val Arg Asp Arg Asp Ala Glu Ile Val Val 175 Lys Asp Asn Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly 185 190 Arg Cys Trp Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr $195 \hspace{1.5cm} 200 \hspace{1.5cm} 205 \hspace{1.5cm}$ Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn 210 215 220 Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp 225 230 235 Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val Pro Arg Cys Pro Gin Pro Leu Val Tyr Asn Lys Leu Thr Phe Gin Leu 260 265 270 Glu Pro Asn Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 275 280 285 Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala Cys Pro Pro Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys 305 310 315 Glu Pro Cys Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser 325 330 335 Gly Ser Arg Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val $340\ , \qquad 345$ Asn Cys Thr Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu 355 360 365 Asn Gly Asp Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu 370 380 Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln 385 400 Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr 405 410 415 Thr Ile Gly Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile 420 425 430 Met Lys Asn Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu 435 440 Ile Ser Ala Gly Arg Ile Tyr Ile Ser Ala Asn Arg Gln Leu Cys Tyr His His Ser Leu Asn Trp Thr Lys Val Leu Arg Gly Pro Thr Glu Glu 465 470 475 480 Arg Leu Asp Ile Lys His Asn Arg Pro Arg Arg Asp Cys Val Ala Glu 485 490 495 Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Gly Gly Val 515 520 525 Cys Val Thr His Cys Asn Phe Leu Asn Gly Glu Pro Arg Glu Phe Ala 530 540 His Glu Ala Glu Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu 545 550 560 Gly Thr Ala Thr Cys Asn Gly Ser Gly Ser Asp Thr Cys Ala Gln Cys 575 Ala His Phe Arg Asp Gly Pro His Cys Val Ser Ser Cys Pro His Gly Val Leu Gly Ala Lys Gly Pro Ile Tyr Lys Tyr Pro Asp Val Gln Asn 595 600 605 Glu Cys Arg Pro Cys His Glu Asn Cys Thr Gln Gly Cys Lys Gly Pro

protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Glu Leu Gln Asp Cys Leu Gly Gln Thr Leu Val Leu Ile Gly Lys Thr 625 630 635 His Leu Thr Met Ala Leu Thr Val Ile Ala Gly Leu Val Val Ile Phe
645 650 655 Met Met Leu Gly Gly Thr Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln 660 665 670 Asn Lys Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu 675 680 685 Pro Leu Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe 690 695 700 Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe 705 710 720 Gly Thr Val His Lys Gly Val Trp Ile Pro Glu Gly Glu Ser Ile Lys 725 730 735 Ile Pro Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser Phe Gln Ala Val Thr Asp His Met Leu Ala Ile Gly Ser Leu Asp His 765 760 765 Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln
770 780 Leu Val Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg 785 790 795 800 Gln His Arg Gly Ala Leu Gly Pro Gln Leu Leu Leu Asn Trp Gly Val 805 810 815 Gln Ile Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Gly Met Val His 820 825 830 Arg Asn Leu Ala Ala Arg Asn Val Leu Leu Lys Ser Pro Ser Gln Val 835 840 845 Gln Val Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys Gln Leu Leu Tyr Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu 865 870 875 Glu Ser Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr $900 \hspace{0.5in} 905$ Ala Gly Leu Arg Leu Ala Glu Val Pro Asp Leu Leu Glu Lys Gly Glu 915 925 Arg Leu Ala Gln Pro Gln Ile Cys Thr Ile Asp Val Tyr Met Val Met 930 940 Val Lys Cys Trp Met Ile Asp Glu Asn Ile Arg Pro Thr Phe Lys Glu 945 950 955

Leu Ala Asn Glu Phe Thr Arg Met Ala Arg Asp Pro Pro Arg Tyr Leu

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 965 970 975

Val Ile Lys Arg Glu Ser Gly Pro Gly Ile Ala Pro Gly Pro 980 985 990

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His Gly Leu Thr Asn Lys Lys Leu Glu Glu Val Glu Leu Glu Pro Glu 995 1000 1005

Leu Asp Leu Asp Leu Asp Leu Glu Ala Glu Glu Asp Asn Leu Ala 1010 1020

Thr Thr Leu Gly Ser Ala Leu Ser Leu Pro Val Gly Thr Leu 1025 1030 1035

Asn Arg Pro Arg Gly Ser Gln Ser Leu Leu Ser Pro Ser Ser Gly 1040 1050

Tyr Met Pro Met Asn Gln Gly Asn Leu Gly Glu Ser Cys Gln Glu 1055 1060 1065

Ser Ala Val Ser Gly Ser Ser Glu Arg Cys Pro Arg Pro Val Ser 1070 1080

Leu His Pro Met Pro Arg Gly Cys Leu Ala Ser Glu Ser Ser Glu 1085 1090 1095

Gly His Val Thr Gly Ser Glu Ala Glu Leu Gln Glu Lys Val Ser 1100 11105

Met Cys Arg Ser Arg Ser Arg Ser Arg Ser Pro Arg Pro Arg Gly

Asp Ser Ala Tyr His Ser Gln Arg His Ser Leu Leu Thr Pro Val 1130 1140

Thr Pro Leu Ser Pro Pro Gly Leu Glu Glu Glu Asp Val Asn Gly 1145 1150

Tyr Val Met Pro Asp Thr His Leu Lys Gly Thr Pro Ser Ser Arg 1160 1165 1170

Glu Gly Thr Leu Ser Ser Val Gly Leu Ser Ser Val Leu Gly Thr $1175 \,$ $1180 \,$ $1185 \,$

Glu Glu Glu Asp Glu Asp Glu Glu Tyr Glu Tyr Met Asn Arg Arg 1190 1200

Arg Arg His Ser Pro Pro His Pro Pro Arg Pro Ser Ser Leu Glu

Glu Leu Gly Tyr Glu Tyr Met Asp Val Gly Ser Asp Leu Ser Ala 1220 1225 1230

Ser Leu Gly Ser Thr Gln Ser Cys Pro Leu His Pro Val Pro Ile 1235 1240 1245

Met Pro Thr Ala Gly Thr Thr Pro Asp Glu Asp Tyr Glu Tyr Met 1250 1260

Asn Arg Gln Arg Asp Gly Gly Gly Pro Gly Gly Asp Tyr Ala Ala 1265 1270 1275

Met Gly Ala Cys Pro Ala Ser Glu Gln Gly Tyr Glu Glu Met Arg

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.5T25.txt Ala Phe Gln Gly Pro Gly His Gln Ala Pro His Val His Tyr Ala

Arg Leu Lys Thr Leu Arg Ser Leu Glu Ala Thr Asp Ser Ala Phe 1310 1320

Asp Asn Pro Asp Tyr Trp His Ser Arg Leu Phe Pro Lys Ala Asn 1325 1330

Ala Gln Arg Thr 1340

<210> 187 <211> 1252 <212> PRT <213> Homo sapiens

Met Ser Thr Thr Val Asn Val Asp Ser Leu Ala Glu Tyr Glu Lys Ser 10 15

Gin Ile Lys Arg Ala Leu Glu Leu Gly Thr Val Met Thr Val Phe Ser

Phe Arg Lys Ser Thr Pro Glu Arg Arg Thr Val Gln Val Ile Met Glu 35 40 45

Thr Arg Gln Val Ala Trp Ser Lys Thr Ala Asp Lys Ile Glu Gly Phe $50 \rm{60}$

Leu Asp Ile Met Glu Ile Lys Glu Ile Arg Pro Gly Lys Asn Ser Lys 65 70 75 80

Asp Phe Glu Arg Ala Lys Ala Val Arg Gln Lys Glu Asp Cys Cys Phe $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95$

Thr Ile Leu Tyr Gly Thr Gln Phe Val Leu Ser Thr Leu Ser Leu Ala $100\,$ $^{\circ}$ $105\,$

Ala Asp Ser Lys Glu Asp Ala Val Asn Trp Leu Ser Gly Leu Lys Ile 115 120 125

Leu His Gln Glu Ala Met Asn Ala Ser Thr Pro Thr Ile Ile Glu Ser

Trp Leu Arg Lys Gln Ile Tyr Ser Val Asp Gln Thr Arg Arg Asn Ser 145 150 155 160

Ile Ser Leu Arg Glu Leu Lys Thr Ile Leu Pro Leu Ile Asn Phe Lys 165 170 175

Val Ser Ser Ala Lys Phe Leu Lys Asp Lys Phe Val Glu Ile Gly Ala 180 185 190

His Lys Asp Glu Leu Ser Phe Glu Gln Phe His Leu Phe Tyr Lys Lys

Leu Met Phe Glu Gln Gln Lys Ser Ile Leu Asp Glu Phe Lys Lys Asp 210 225 220

Ser Ser val Phe Ile Leu Gly Asn Thr Asp Arg Pro Asp Ala Ser Ala 225 230 235 240

Val Tyr Leu His Asp Phe Gln Arg Phe Leu Ile His Glu Gln Glu 245 250 255



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Trp Ala Gln Asp Leu Asn Lys Val Arg Glu Arg Met Thr Lys Phe Ile Asp Asp Thr Met Arg Glu Thr Ala Glu Pro Phe Leu Phe Val Asp 275 280 285 Glu Phe Leu Thr Tyr Leu Phe Ser Arg Glu Asn Ser Ile Trp Asp Glu 290 295 300 Lys Tyr Asp Ala Val Asp Met Gln Asp Met Asn Asn Pro Leu Ser His 305 310 315 Tyr Trp Ile Ser Ser Ser His Asn Thr Tyr Leu Thr Gly Asp Gln Leu 325 330 335 Arg Ser Glu Ser Ser Pro Glu Ala Tyr Ile Arg Cys Leu Arg Met Gly Cys Arg Cys Ile Glu Leu Asp Cys Trp Asp Gly Pro Asp Gly Lys Pro Val lle Tyr His Gly Trp Thr Arg Thr Thr Lys Ile Lys Phe Asp Asp $370 \hspace{1cm} 375 \hspace{1cm} 380$ val val Gln Ala Ile Lys Asp His Ala Phe Val Thr Ser Ser Phe Pro 385 390 395 400 Val Ile Leu Ser Ile Glu Glu His Cys Ser Val Glu Gln Gln Arg His 405 410 415 Met Ala Lys Ala Phe Lys Glu Val Phe Gly Asp Leu Leu Leu Thr Lys 420 430 Pro Thr Glu Ala Ser Ala Asp Gln Leu Pro Ser Pro Ser Gln Leu Arg 435 440 445 Glu Lys Ile Ile Lys His Lys Lys Leu Gly Pro Arg Gly Asp Val 450 455 460 Asp Val Asn Met Glu Asp Lys Lys Asp Glu His Lys Gln Gln Glu 465 470 475 480 Leu Tyr Met Trp Asp Ser Ile Asp Gln Lys Trp Thr Arg His Tyr Cys
485 490 495 Ala Ile Ala Asp Ala Lys Leu Ser Phe Ser Asp Asp Ile Glu Gln Thr 500 505 510 Met Glu Glu Val Pro Gln Asp Ile Pro Pro Thr Glu Leu His Phe 515 520 525 Gly Glu Lys Trp Phe His Lys Lys Val Glu Lys Arg Thr Ser Ala Glu Lys Leu Leu Gln Glu Tyr Cys Met Glu Thr Gly Gly Lys Asp Gly Thr 545 550 560Phe Leu Val Arg Glu Ser Glu Thr Phe Pro Asn Asp Tyr Thr Leu Ser 565 570 575 Phe Trp Arg Ser Gly Arg Val Gln His Cys Arg Ile Arg Ser Thr Met 580



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Glu Gly Gly Thr Leu Lys Tyr Tyr Leu Thr Asp Asn Leu Arg Phe Arg
595 600 605

Arg Met Tyr Ala Leu Île Gln His Tyr Arg Glu Thr His Leu Pro Cys 610 620 Ala Glu Phe Glu Leu Arg Leu Thr Asp Pro Val Pro Asn Pro Asn Pro 625 630 635 His Glu Ser Lys Pro Trp Tyr Tyr Asp Ser Leu Ser Arg Gly Glu Ala 645 650 655 Glu Asp Met Leu Met Arg Ile Pro Arg Asp Gly Ala Phe Leu Ile Arg 660 665 670 Lys Arg Glu Gly Ser Asp Ser Tyr Ala Ile Thr Phe Arg Ala Arg Gly
675 680 685 Lys Val Lys His Cys Arg Ile Asn Arg Asp Gly Arg His Phe Val Leu 690 700Gly Thr Ser Ala Tyr Phe Glu Ser Leu Val Glu Leu Val Ser Tyr Tyr 705 710 715 720 Glu Lys His Ser Leu Tyr Arg Lys Met Arg Leu Arg Tyr Pro Val Thr Pro Glu Leu Leu Glu Arg Tyr Asn Thr Glu Arg Asp Ile Asn Ser Leu 740 745 750 Tyr Asp Val Ser Arg Met Tyr Val Asp Pro Ser Glu Ile Asn Pro Ser 755 760 765 Met Pro Gln Arg Thr Val Lys Ala Leu Tyr Asp Tyr Lys Ala Lys Arg Ser Asp Glu Leu Ser Phe Cys Arg Gly Ala Leu Ile His Asn Val Ser 785 790 795 800 Lys Glu Pro Gly Gly Trp Trp Lys Gly Asp Tyr Gly Thr Arg Ile Gln 805 810 815 Gln Tyr Phe Pro Ser Asn Tyr Val Glu Asp Ile Ser Thr Ala Asp Phe 820 825 830 Glu Glu Leu Glu Lys Gln Ile Ile Glu Asp Asn Pro Leu Gly Ser Leu 835 840 . 845 Cys Arg Gly Ile Leu Asp Leu Asn Thr Tyr Asn Val Val Lys Ala Pro Gln Gly Lys Asn Gln Lys Ser Phe Val Phe Ile Leu Glu Pro Lys Glu 865 870 875 880 Gln Gly Asp Pro Pro Val Glu Phe Ala Thr Asp Arg Val Glu Glu Leu 885 890 895 Phe Glu Trp Phe Gln Ser Ile Arg Glu Ile Thr Trp Lys Ile Asp Ser 900 905Lys Glu Asn Asn Met Lys Tyr Trp Glu Lys Asn Gln Ser Ile Ala Ile 915 920 925 Glu Leu Ser Asp Leu Val Val Tyr Cys Lys Pro Thr Ser Lys Thr Lys

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Asp Asn Leu Glu Asn Pro Asp Phe Arg Glu Ile Arg Ser Phe Val Glu Thr Lys Ala Asp Ser Ile Ile Arg Gln Lys Pro Val Asp Leu Leu Lys 965 970 975 Tyr Asn Gln Lys Gly Leu Thr Arg Val Tyr Pro Lys Gly Gln Arg Val 980 985 990 Asp Ser Ser Asn Tyr Asp Pro Phe Arg Leu Trp Leu Cys Gly Ser Gln $995 \hspace{1cm} 1000 \hspace{1cm} 1005$ Met Val Ala Leu Asn Phe Gln Thr Ala Asp Lys Tyr Met Gln Met 1010 1020 Asn His Ala Leu Phe Ser Leu Asn Gly Arg Thr Gly Tyr Val Leu 1025 1030 1035 Gln Pro Glu Ser Met Arg Thr Glu Lys Tyr Asp Pro Met Pro Pro 1040 1050 Glu Ser Gln Arg Lys Ile Leu Met Thr Leu Thr Val Lys Val Leu 1055 1060 1065 Gly Ala Arg His Leu Pro Lys Leu Gly Arg Ser Ile Ala Cys Pro 1070 1080 Phe Val Glu Val Glu Ile Cys Gly Ala Glu Tyr Gly Asn Asn Lys 1085 1090 1095 Phe Lys Thr Thr Val Val Asn Asp Asn Gly Leu Ser Pro Ile Trp 1100 1105 1110 Ala Pro Thr Gln Glu Lys Val Thr Phe Glu Ile Tyr Asp Pro Asn 1115 1120 1125 Leu Ala Phe Leu Arg Phe Val Val Tyr Glu Glu Asp Met Phe Ser 1130 1140 Asp Pro Asn Phe Leu Ala His Ala Thr Tyr Pro Ile Lys Ala Val 1145 1150 1155 Lys Ser Gly Phe Arg Ser Val Pro Leu Lys Asn Gly Tyr Ser Glu 1160 1170Asp Ile Glu Leu Ala Ser Leu Leu Val Phe Cys Glu Met Arg Pro 1175 1180 1185 Val Leu Glu Ser Glu Glu Glu Leu Tyr Ser Ser Cys Arg Gln Leu 1190 1195 1200 Arg Arg Arg Gln Glu Glu Leu Asn Asn Gln Leu Phe Leu Tyr Asp 1205 1210 1215 Thr His Gln Asn Leu Arg Asn Ala Asn Arg Asp Ala Leu Val Lys 1220 1230 Glu Phe Ser Val Asn Glu Asn His Ser Ser Cys Thr Arg Arg Asn 1235 1240 1245 Ala Thr Arg Gly 1250

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt <210> <211> <212> <213>

Homo sapiens

<400> 188

Met Ala Gly Asn Val Lys Lys Ser Ser Gly Ala Gly Gly Gly Thr Gly 1 10 15

Ser Gly Gly Ser Gly Ser Gly Gly Leu Ile Gly Leu Met Lys Asp Ala 20 25

Phe Gln Pro His His His His His Leu Ser Pro His Pro Pro 35 40 45

Gly Thr Val Asp Lys Lys Met Val Glu Lys Cys Trp Lys Leu Met Asp 50 60

Lys Val Val Arg Leu Cys Gln Asn Pro Lys Leu Ala Leu Lys Asn Ser 65 70 75 80

Pro Pro Tyr Ile Leu Asp Leu Leu Pro Asp Thr Tyr Gln His Leu Arg 90 95

Thr Ile Leu Ser Arg Tyr Glu Gly Lys Met Glu Thr Leu Gly Glu Asn 100 105 110

Glu Tyr Phe Arg Val Phe Met Glu Asn Leu Met Lys Lys Thr Lys Gln 115 120 125

Thr Ile Ser Leu Phe Lys Glu Gly Lys Glu Arg Met Tyr Glu Glu Asn 130 135 140

Ser Gln Pro Arg Arg Asn Leu Thr Lys Leu Ser Leu Ile Phe Ser His 145 150 155 160

Met Leu Ala Glu Leu Lys Gly Ile Phe Pro Ser Gly Leu Phe Gln Gly 165 170 175

Asp Thr Phe Arg Ile Thr Lys Ala Asp Ala Ala Glu Phe Trp Arg Lys 180 185 190

Ala Phe Gly Glu Lys Thr Ile Val Pro Trp Lys Ser Phe Arg Gln Ala 195 200 205

Leu His Glu Val His Pro Ile Ser Ser Gly Leu Glu Ala Met Ala Leu 210 220

Lys Ser Thr Ile Asp Leu Thr Cys Asm Asp Tyr Ile Ser Val Phe Glu 225 230 235

Phe Asp Ile Phe Thr Arg Leu Phe Gln Pro Trp Ser Ser Leu Leu Arg 245 250 255

Asn Trp Asn Ser Leu Ala Val Thr His Pro Gly Tyr Met Ala Phe Leu 265 270

Thr Tyr Asp Glu Val Lys Ala Arg Leu Gln Lys Phe Ile His Lys Pro 275 280 285

Gly Ser Tyr Ile Phe Arg Leu Ser Cys Thr Arg Leu Gly Gln Trp Ala 290 295 300

Ile Gly Tyr Val Thr Ala Asp Gly Asn Ile Leu Gln Thr Ile Pro His 305 310 315



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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt

Asn Lys Pro Leu Phe Gln Ala Leu Ile Asp Gly Phe Arg Glu Gly Phe
325
330
335

Tyr Leu Phe Pro Asp Gly Arg Asn Gln Asn Pro Asp Leu Thr Gly Leu 340 350 Cys Glu Pro Thr Pro Gln Asp His Ile Lys Val Thr Gln Glu Gln Tyr 355 360 365 Glu Leu Tyr Cys Glu Met Gly Ser Thr Phe Gln Leu Cys Lys Ile Cys 370 380Ala Glu Asn Asp Lys Asp Val Lys Ile Glu Pro Cys Gly His Leu Met $385 \hspace{1.5cm} 390 \hspace{1.5cm} 395 \hspace{1.5cm} 400$ Cys Thr Ser Cys Leu Thr Ser Trp Gln Glu Ser Glu Gly Gln Gly Cys 405 410 415 Pro Phe Cys Arg Cys Glu Ile Lys Gly Thr Glu Pro Ile Val Val Asp 420 425 430 Pro Phe Asp Pro Arg Gly Ser Gly Ser Leu Leu Arg Gln Gly Ala Glu 435 445Gly Ala Pro Ser Pro Asn Tyr Asp Asp Asp Asp Glu Arg Ala Asp 450 460 Asp Thr Leu Phe Met Met Lys Glu Leu Ala Gly Ala Lys Val Glu Arg 465 470 475 Pro Pro Ser Pro Phe Ser Met Ala Pro Gln Ala Ser Leu Pro Pro Val 485 490 495 Pro Pro Arg Leu Asp Leu Leu Pro Gln Arg Val Cys Val Pro Ser Ser 500 505 Ala Ser Ala Leu Gly Thr Ala Ser Lys Ala Ala Ser Gly Ser Leu His 515 525 Lys Asp Lys Pro Leu Pro Val Pro Pro Thr Leu Arg Asp Leu Pro Pro 530 540 Pro Pro Pro Asp Arg Pro Tyr Ser Val Gly Ala Glu Ser Arg Pro 545 550 555 Gln Arg Arg Pro Leu Pro Cys Thr Pro Gly Asp Cys Pro Ser Arg Asp 565 570 Lys Leu Pro Pro Val Pro Ser Ser Arg Leu Gly Asp Ser Trp Leu Pro 580 585 Arg Pro Ile Pro Lys Val Pro Val Ser Ala Pro Ser Ser Ser Asp Pro 595 605Trp Thr Gly Arg Glu Leu Thr Asn Arg His Ser Leu Pro Phe Ser Leu 610 620 Pro Ser Gln Met Glu Pro Arg Pro Asp Val Pro Arg Leu Gly Ser Thr 625 630 635 Phe Ser Leu Asp Thr Ser Met Ser Met Asn Ser Ser Pro Leu Val Gly 655

Pro Glu Cys Asp His Pro Lys Ile Lys Pro Ser Ser Ala Asn Ala

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 660 665 670 The Tyr Ser Leu Ala Ala Arg Pro Leu Pro Val Pro Lys Leu Pro Pro Gly Glu Gln Cys Glu Gly Glu Glu Asp Thr Glu Tyr Met Thr Pro Ser 690 695 700 Ser Arg Pro Leu Arg Pro Leu Asp Thr Ser Gln Ser Ser Arg Ala Cys 705 710 715 720 Asp Cys Asp Gln Gln Ile Asp Ser Cys Thr Tyr Glu Ala Met Tyr Asn 725 730 735

Ile Gln Ser Gln Ala Pro Ser Ile Thr Glu Ser Ser Thr Phe Gly Glu
740 745 750 Gly Asn Leu Ala Ala Ala His Ala Asn Thr Gly Pro Glu Glu Ser Glu 755 760 765 Asn Glu Asp Asp Gly Tyr Asp Val Pro Lys Pro Pro Val Pro Ala Val Leu Ala Arg Arg Thr Leu Ser Asp Ile Ser Asn Ala Ser Ser Ser Phe Gly Trp Leu Ser Leu Asp Gly Asp Pro Thr Thr Asn Val Thr Glu Gly $805 \ \ 810 \ \ 815$ Ser Gln Val Pro Glu Arg Pro Pro Lys Pro Phe Pro Arg Arg Ile Asn 820 825 Ser Glu Arg Lys Ala Gly Ser Cys Gln Gln Gly Ser Gly Pro Ala Ala 835 840 845 Ser Ala Ala Thr Ala Ser Pro Gln Leu Ser Ser Glu Ile Glu Asn Leu 850 855 860

Met Ser Gln Gly Tyr Ser Tyr Gln Asp Ile Gln Lys Ala Leu Val Ile 865 870 875 880

Ala Gln Asn Asn Ile Glu Met Ala Lys Asn Ile Leu Arg Glu Phe Val

Ser Ile Ser Ser Pro Ala His Val Ala Thr

Met Ala Ser Pro Pro Glu Ser Asp Gly Phe Ser Asp Val Arg Lys Val

Gly Tyr Leu Arg Lys Pro Lys Ser Met His Lys Arg Phe Phe Val Leu 20 25 30

Arg Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu

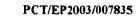
ASN Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile

<210> 189 <211> 1242 <212> PRT <213> Homo sapiens

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Pro Leu Glu Ser Cys Phe Asn Ile Asn Lys Arg Ala Asp Ser Lys Asn
65 70 75 80

Lys His Leu Val Ala Leu Tyr Thr Arg Asp Glu His Phe Ala Ile Ala 85 90 95 Ala Asp Ser Glu Ala Glu Gln Asp Ser Trp Tyr Gln Ala Leu Leu Gln 100 105 110 Leu His Asn Arg Ala Lys Gly His His Asp Gly Ala Ala Ala Leu Gly 115 120 125 Ala Gly Gly Gly Gly Ser Cys Ser Gly Ser Ser Gly Leu Gly Glu 130 140 Ala Gly Glu Asp Leu Ser Tyr Gly Asp Val Pro Pro Gly Pro Ala Phe 145 150 155 160 Lys Glu Val Trp Gln Val Ile Leu Lys Pro Lys Gly Leu Gly Gln Thr 165 170 175 Lys Asn Leu Ile Gly Ile Tyr Arg Leu Cys Leu Thr Ser Lys Thr Ile 180 185 190 Ser Phe Val Lys Leu Asn Ser Glu Ala Ala Ala Val Val Leu Gln Leu 195 200 205 Met Asn Ile Arg Arg Cys Gly His Ser Glu Asn Phe Phe Phe Ile Glu 210 220 Val Gly Arg Ser Ala Val Thr Gly Pro Gly Glu Phe Trp Met Gln Val 225 230 235 Asp Asp Ser Val Val Ala Gln Asn Met His Glu Thr Ile Leu Glu Ala 245 250 255 Met Arg Ala Met Ser Asp Glu Phe Arg Pro Arg Ser Lys Ser Gln Ser 265 Ser Ser Asn Cys Ser Asn Pro Ile Ser Val Pro Leu Arg Arg His His 275 280 285 Leu Asn Asn Pro Pro Pro Ser Gln Val Gly Leu Thr Arg Arg Ser Arg 290 295 300 Thr Glu Ser Ile Thr Ala Thr Ser Pro Ala Ser Met Val Gly Gly Lys 305 310 315 Pro Gly Ser Phe Arg Val Arg Ala Ser Ser Asp Gly Glu Gly Thr Met 325 330 335 Ser Arg Pro Ala Ser Val Asp Gly Ser Pro Val Ser Pro Ser Thr Asn 340 345 Arg Thr His Ala His Arg His Arg Gly Ser Ala Arg Leu His Pro Pro 355 360Leu Asn His Ser Arg Ser Ile Pro Met Pro Ala Ser Arg Cys Ser Pro Ser Ala Thr Ser Pro Val Ser Leu Ser Ser Ser Ser Thr Ser Gly His 385 390 395 Gly Ser Thr Ser Asp Cys Leu Phe Pro Arg Arg Ser Ser Ala Ser Val 405 410 415



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Gly Ser Pro Ser Asp Gly Gly Phe Ile Ser Ser Asp Glu Tyr Gly
420
425 Ser Ser Pro Cys Asp Phe Arg Ser Ser Phe Arg Ser Val Thr Pro Asp Ser Leu Gly His Thr Pro Pro Ala Arg Gly Glu Glu Glu Leu Ser Asn 450 455 460 Tyr Ile Cys Met Gly Gly Lys Gly Pro Ser Thr Leu Thr Ala Pro Asn 465 470 475 480 Gly His Tyr Ile Leu Ser Arg Gly Gly Asn Gly His Arg Cys Thr Pro 485 490 495 Gly Thr Gly Leu Gly Thr Ser Pro Ala Leu Ala Gly Asp Glu Ala Ala 500 505 510 Ser Ala Ala Asp Leu Asp Asn Arg Phe Arg Lys Arg Thr His Ser Ala 515 520 525 Gly Thr Ser Pro Thr Ile Thr His Gln Lys Thr Pro Ser Gln Ser Ser 530 540 Val Ala Ser Ile Glu Glu Tyr Thr Glu Met Met Pro Ala Tyr Pro Pro 545 550 560 Gly Gly Gly Ser Gly Gly Arg Leu Pro Gly His Arg His Ser Ala Phe Val Pro Thr Arg Ser Tyr Pro Glu Glu Glu Leu Glu Met His Pro Leu 580 585 590 Glu Arg Arg Gly Gly His His Arg Pro Asp Ser Ser Thr Leu His Thr Asp Asp Gly Tyr Met Pro Met Ser Pro Gly Val Ala Pro Val Pro Ser 610 620 Gly Arg Lys Gly Ser Gly Asp Tyr Met Pro Met Ser Pro Lys Ser Val 625 630 635 Ser Ala Pro Gln Gln Ile Ile Asn Pro Ile Arg Arg His Pro Gln Arg 645 650 655 Val Asp Pro Asn Gly Tyr Met Met Met Ser Pro Ser Gly Gly Cys Ser 660 665 670 Pro Asp Ile Gly Gly Gly Pro Ser Ser Ser Ser Ser Ser Ser Asn Ala 675 680 685 Val Pro Ser Gly Thr Ser Tyr Gly Lys Leu Trp Thr Asn Gly Val Gly Gly His His Ser His Val Leu Pro His Pro Lys Pro Pro Val Glu Ser 705 710 720 Ser Gly Gly Lys Leu Leu Pro Cys Thr Gly Asp Tyr Met Asn Met Ser 730 735 Pro Val Gly Asp Ser Asn Thr Ser Ser Pro Ser Asp Cys Tyr Tyr Gly

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt
Pro Glu Asp Pro Gln His Lys Pro Val Leu Ser Tyr Tyr Ser Leu Pro
755 760 765

Arg Ser Phe Lys His Thr Gln Arg Pro Gly Glu Pro Glu Glu Gly Ala 770 780 Arg His Gln His Leu Arg Leu Ser Thr Ser Ser Gly Arg Leu Leu Tyr 785 790 795 800 Ala Ala Thr Ala Asp Asp Ser Ser Ser Ser Thr Ser Ser Asp Ser Leu 805 810 815 Gly Gly Gly Tyr Cys Gly Ala Arg Leu Glu Pro Ser Leu Pro His Pro 820 825 830 His His Gln Val Leu Gln Pro His Leu Pro Arg Lys Val Asp Thr Ala 835 840 845 Ala Gln Thr Asn Ser Arg Leu Ala Arg Pro Thr Arg Leu Ser Leu Gly 850 860 Asp Pro Lys Ala Ser Thr Leu Pro Arg Ala Arg Glu Gln Gln Gln 865 870 880 Gln Gln Pro Leu Leu His Pro Pro Glu Pro Lys Ser Pro Gly Glu Tyr 885 890 895 Val Asn Ile Glu Phe Gly Ser Asp Gln Ser Gly Tyr Leu Ser Gly Pro 900 905 910 Val Ala Phe His Ser Ser Pro Ser Val Arg Cys Pro Ser Gln Leu Gln 915 920 925 Pro Ala Pro Arg Glu Glu Glu Thr Gly Thr Glu Glu Tyr Met Lys Met Asp Leu Gly Pro Gly Arg Arg Ala Ala Trp Gln Glu Ser Thr Gly Val 945 950 955 Glu Met Gly Arg Leu Gly Pro Ala Pro Pro Gly Ala Ala Ser Ile Cys 965 970 975 Arg Pro Thr Arg Ala Val Pro Ser Ser Arg Gly Asp Tyr Met Thr Met 980 985 990 Gln Met Ser Cys Pro Arg Gln Ser Tyr Val Asp Thr Ser Pro Ala Ala 995 1000 1005 Pro Val Ser Tyr Ala Asp Met Arg Thr Gly Ile Ala Ala Glu Glu 1010 1020Val Ser Leu Pro Arg Ala Thr Met Ala Ala Ser Ser Ser Ser 1025 1030 1035 Ala Ala Ser Ala Ser Pro Thr Gly Pro Gln Gly Ala Ala Glu Leu 1040 1045 1050 Ala Ala His Ser Ser Leu Leu Gly Gly Pro Gln Gly Pro Gly Gly 1055 1065 Met Ser Ala Phe Thr Arg Val Asn Leu Ser Pro Asn Arg Asn Gln 1070 1080 Ser Ala Lys Val Ile Arg Ala Asp Pro Gln Gly Cys Arg Arg Arg 1085 1095

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protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt His Ser Ser Glu Thr Phe Ser Ser Thr Pro Ser Ala Thr Arg Val Gly Asn Thr Val Pro Phe Gly Ala Gly Ala Ala Val Gly Gly Gly 1115 1120 1125 Gly Gly Ser Ser Ser Ser Ser Glu Asp Val Lys Arg His Ser Ser 1130 1140 Ala Ser Phe Glu Asn Val Trp Leu Arg Pro Gly Glu Leu Gly Gly 1145 1150 Ala Pro Lys Glu Pro Ala Lys Leu Cys Gly Ala Ala Gly Gly Leu 1160 1165 1170 Glu Asn Gly Leu Asn Tyr Ile Asp Leu Asp Leu Val Lys Asp Phe 1175 1180 1185 Lys Gln Cys Pro Gln Glu Cys Thr Pro Glu Pro Gln Pro Pro Pro 1190 1200 Pro Pro Pro Pro His Gln Pro Leu Gly Ser Gly Glu Ser Ser Ser 1205 1215 Thr Arg Arg Ser Ser Glu Asp Leu Ser Ala Tyr Ala Ser Ile Ser 1220 1225 1230 Phe Gln Lys Gln Pro Glu Asp Arg Gln 1235

<210> 190 <211> 1324 <212> PRT <213> Homo sapiens

<400> 190

Met Ala Ser Pro Pro Arg His Gly Pro Pro Gly Pro Ala Ser Gly Asp

Gly Pro Asn Leu Asn Asn Asn Asn Asn Asn Asn His Ser Val Arg

Lys Cys Gly Tyr Leu Arg Lys Gln Lys His Gly His Lys Arg Phe Phe 35 45

Val Leu Arg Gly Pro Gly Ala Gly Gly Asp Lys Ala Thr Ala Gly Gly 50 60

Gly Ser Ala Pro Gln Pro Pro Arg Leu Glu Tyr Tyr Glu Ser Glu Lys 65 75 80

Asn Trp Arg Ser Lys Ala Gly Ala Pro Lys Arg Val Ile Ala Leu Asp $90 \hspace{1cm} 95$

Cys Cys Leu Asn Ile Asn Lys Arg Ala Asp Pro Lys His Lys Tyr Leu $100 \hspace{1cm} 105 \hspace{1cm} 110$

Ile Ala Leu Tyr Thr Lys Asp Glu Tyr Phe Ala Val Ala Ala Glu Asn 115 125

Glu Gln Glu Gln Glu Gly Trp Tyr Arg Ala Leu Thr Asp Leu Val Ser 130 135 140

Glu Gly Arg Ala Ala Ala Gly Asp Ala Pro Pro Ala Ala Ala Pro Ala



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 145 150 160 Ala Ser Cys Ser Ala Ser Leu Pro Gly Ala Val Gly Gly Ser Ala Gly
170
175 Ala Ala Gly Ala Glu Asp Ser Tyr Gly Leu Val Ala Pro Ala Thr Ala 180 185 190 Ala Tyr Arg Glu Val Trp Gln Val Asn Leu Lys Pro Lys Gly Leu Gly 195 200 205 Gln Ser Lys Asn Leu Thr Gly Val Tyr Arg Leu Cys Leu Ser Ala Arg Thr Ile Gly Phe Val Lys Leu Asn Cys Glu Gln Pro Ser Val Thr Leu 225 230 235 240 Gln Leu Met Asn Ile Arg Arg Cys Gly His Ser Asp Ser Phe Phe Phe 245 250 250Ile Glu Val Gly Arg Ser Ala Val Thr Gly Pro Gly Glu Leu Trp Met 260 265 270 Gln Ala Asp Asp Ser Val Val Ala Gln Asn Ile His Glu Thr Ile Leu 275 280 285 Glu Ala Met Lys Ala Leu Lys Glu Leu Phe Glu Phe Arg Pro Arg Ser 290 295 300 Lys Ser Gln Ser Ser Gly Ser Ser Ala Thr His Pro Ile Ser Val Pro 305 310 315 Gly Ala Arg Arg His His Leu Val Asn Leu Pro Pro Ser Gln Thr 325 330 335 Gly Leu Val Arg Arg Ser Arg Thr Asp Ser Leu Ala Ala Thr Pro Pro 340 345 350 Ala Ala Lys Cys Ser Ser Cys Arg Val Arg Thr Ala Ser Glu Gly Asp $355 \hspace{1cm} 360 \hspace{1cm} 365$ Gly Gly Ala Ala Gly Ala Ala Ala Gly Ala Arg Pro Val Ser 370 380 Val Ala Gly Ser Pro Leu Ser Pro Gly Pro Val Arg Ala Pro Leu Ser 385 390 395 400 Arg Ser His Thr Leu Ile Gly Gly Cys Arg Ala Ala Gly Thr Lys Trp 405 410 415 His Cys Phe Pro Ala Gly Gly Gly Leu Gln His Ser Arg Ser Met Ser 420 425 430 Met Pro Val Glu His Leu Pro Pro Ala Ala Thr Ser Pro Gly Ser Leu 435 440 445 Ser Ser Ser Asp His Gly Trp Gly Ser Tyr Pro Pro Pro Pro Gly 450 455 460 Pro His Pro Leu Leu Pro His Pro Leu His His Gly Pro Gly Gln Arg 465 470 475 480 Pro Ser Ser Gly Ser Ala Ser Ala Ser Gly Ser Pro Ser Asp Pro Gly 485 490 495



WO 2004/009622 PCT/EP2003/007835 Protein complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Phe Met Ser Leu Asp Glu Tyr Gly Ser Ser Pro Gly Asp Leu Arg Ala 500 505 510 Phe Cys Ser His Arg Ser Asn Thr Pro Glu Ser Ile Ala Glu Thr Pro 515 520 525 Pro Ala Arg Asp Gly Gly Gly Gly Glu Phe Tyr Gly Tyr Met Thr Met Asp Arg Pro Leu Ser His Cys Gly Arg Ser Tyr Arg Arg Val Ser 545 550 555 · 560 Gly Asp Ala Ala Gln Asp Leu Asp Arg Gly Leu Arg Lys Arg Thr Tyr 565 570 Ser Leu Thr Thr Pro Ala Arg Gln Arg Pro Val Pro Gln Pro Ser Ser 585 590 Ala Ser Leu Asp Glu Tyr Thr Leu Met Arg Ala Thr Phe Ser Gly Ser Ala Gly Arg Leu Cys Pro Ser Cys Pro Ala Ser Ser Pro Lys Val Ala 610 620 Tyr His Pro Tyr Pro Glu Asp Tyr Gly Asp Ile Glu Ile Gly Ser His 625 630 635 Arg Ser Ser Ser Asn Leu Gly Ala Asp Asp Gly Tyr Met Pro Met
645 650 Thr Pro Gly Ala Ala Leu Ala Gly Ser Gly Ser Gly Ser Cys Arg Ser 660 665 670 Asp Asp Tyr Met Pro Met Ser Pro Ala Ser Val Ser Ala Pro Lys Gln 675 685Ile Leu Gln Pro Arg Ala Ala Ala Ala Ala Ala Ala Val Pro Phe 690 695 700

Pro Glu Asp Ser Gly Tyr Met Arg Met Trp Cys Gly Ser Lys Leu Ser 740 745 750 Met Glu His Ala Asp Gly Lys Leu Leu Pro Asn Gly Asp Tyr Leu Asn 755 760 765 Val Ser Pro Ser Asp Ala Val Thr Thr Gly Thr Pro Pro Asp Phe Phe 770 780 Ser Ala Ala Leu His Pro Gly Gly Glu Pro Leu Arg Gly Val Pro Gly 785 790 795 800

Ala Gly Pro Ala Gly Pro Ala Pro Thr Phe Ala Ala Gly Arg Thr Phe 705 710 725

Pro Ala Ser Gly Gly Tyr Lys Ala Ser Ser Pro Ala Glu Ser Ser 725 730 735

Gly Gly Asp Ser Asp Gln Tyr Val Leu Met Ser Ser Pro Val Gly Arg

Cys Cys Tyr Ser Ser Leu Pro Arg Ser Tyr Lys Ala Pro Tyr Thr Cys 805 810 815

Ile Leu Glu Glu Glu Arg Leu Glu Pro Gln Ala Thr Pro Gly Pro Thr



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 835 840 845

Gln Ala Ala Ser Ala Phe Gly Ala Gly Pro Thr Gln Pro Pro His Pro 850 855

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Val Val Pro Ser Pro Val Arg Pro Ser Gly Gly Arg Pro Glu Gly Phe 865 870 875

Leu Gly Gln Arg Gly Arg Ala Val Arg Pro Thr Arg Leu Ser Leu Glu

Gly Leu Pro Ser Leu Pro Ser Met His Glu Tyr Pro Leu Pro Pro Glu 900 905 910

Pro Lys Ser Pro Gly Glu Tyr Ile Asn Ile Asp Phe Gly Glu Pro Gly 915 920 925

Ala Arg Leu Ser Pro Pro Ala Pro Pro Leu Leu Ala Ser Ala Ala Ser 930 940

Ser Ser Ser Leu Leu Ser Ala Ser Ser Pro Ala Leu Ser Leu Gly Ser 945 950 955 960

Gly Thr Pro Gly Thr Ser Ser Asp Ser Arg Gln Arg Ser Pro Leu Ser 965 970 975

Asp Tyr Met Asn Leu Asp Phe Ser Ser Pro Lys Ser Pro Lys Pro Gly 980 985

Ala Pro Ser Gly His Pro Val Gly Ser Leu Asp Gly Leu Leu Ser Pro 995 1000 1005

Glu Ala Ser Ser Pro Tyr Pro Pro Leu Pro Pro Arg Pro Ser Ala 1010 1015 1020

Ser Pro Ser Ser Ser Leu Gln Pro Pro Pro Pro Pro Pro Ala Pro 1025 1035

Gly Glu Leu Tyr Arg Leu Pro Pro Ala Ser Ala Val Ala Thr Ala 1040 1050

Gln Gly Pro Gly Ala Ala Ser Ser Leu Ser Ser Asp Thr Gly Asp 1055 1066

Asn Gly Asp Tyr Thr Glu Met Ala Phe Gly Val Ala Ala Thr Pro 1070 1080

Pro Gln Pro Ile Ala Ala Pro Pro Lys Pro Glu Ala Ala Arg Val 1085 1090 1095

Ala Ser Pro Thr Ser Gly Val Lys Arg Leu Ser Leu Met Glu Gln 1100 1110

Val Ser Gly Val Glu Ala Phe Leu Gln Ala Ser Gln Pro Pro Asp 1115 1120 1125

Pro His Arg Gly Ala Lys Val Ile Arg Ala Asp Pro Gln Gly Gly 1130 1140

Arg Arg Arg His Ser Ser Glu Thr Phe Ser Ser Thr Thr Thr Val

Thr pro Val Ser Pro Ser Phe Ala His Asn Pro Lys Arg His Asn 1160 1170 1170

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Ala Ser Val Glu Asn Val Ser Leu Arg Lys Ser Ser Glu Gly 1175 1180 1185

Gly Val Gly Val Gly Pro Gly Gly Gly Asp Glu Pro Pro Thr Ser

Pro Arg Gln Leu Gln Pro Ala Pro Pro Leu Ala Pro Gln Gly Arg 1205 1210 1215

Pro Trp Thr Pro Gly Gln Pro Gly Gly Leu Val Gly Cys Pro Gly 1220 1230

Ser Gly Gly Ser Pro Met Arg Arg Glu Thr Ser Ala Gly Phe Gln 1235 1240 1245

Asn Gly Leu Lys Tyr Ile Ala Ile Asp Val Arg Glu Glu Pro Gly 1250 1260

Leu Pro Pro Gln Pro Gln Pro Pro Pro Pro Leu Pro Gln Pro 1265 1270 1275

Gly Asp Lys Ser Ser Trp Gly Arg Thr Arg Ser Leu Gly Gly Leu 1280 1285 1290

Ile Ser Ala Val Gly Val Gly Ser Thr Arg Gly Gly Cys Gly Gly 1295 1300 1305

Pro Gly Pro Gly Ala Pro Ala Pro Cys Pro Thr Thr Tyr Ala Gln
1310 1320

нis

<210> 191 <211> 168 <212> PRT <213> Homo

Homo sapiens

Met Phe Gln Ile Pro Glu Phe Glu Pro Ser Glu Gln Glu Asp Ser Ser 1 10 15

Ser Ala Glu Arg Gly Leu Gly Pro Ser Pro Ala Gly Asp Gly Pro Ser

Gly Ser Gly Lys His His Arg Gln Ala Pro Gly Leu Leu Trp Asp Ala

Ser His Gln Gln Gln Pro Thr Ser Ser His His Gly Gly Ala

Gly Ala Val Glu Ile Arg Ser Arg His Ser Ser Tyr Pro Ala Gly Thr

Glu Asp Asp Glu Gly Met Gly Glu Glu Pro Ser Pro Phe Arg Gly Arg

Ser Arg Ser Ala Pro Pro Asn Leu Trp Ala Ala Gln Arg Tyr Gly Arg

Glu Leu Arg Arg Met Ser Asp Glu Phe Val Asp Ser Phe Lys Lys Gly

Leu pro Arg Pro Lys Ser Ala Gly Thr Ala Thr Gln Met Arg Gln Ser

WO 2004/009622 PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Ser Trp Thr Arg Val Phe Gln Ser Trp Trp Asp Arg Asn Leu Gly Arg Gly Ser Ser Ala Pro Ser Gln 165

Homo sapiens

Met Thr Thr Ser Ala Ser Ser His Leu Asn Lys Gly Ile Lys Gln Val Tyr Met Ser Leu Pro Gln Gly Glu Lys Val Gln Ala Met Tyr Ile Trp Ile Asp Gly Thr Gly Glu Gly Leu Arg Cys Lys Thr Arg Thr Leu Asp Ser Glu Pro Lys Cys Val Glu Glu Leu Pro Glu Trp Asn Phe Asp Gly 50 60 Ser Ser Thr Leu Gln Ser Glu Gly Ser Asn Ser Asp Met Tyr Leu Val Pro Ala Ala Met Phe Arg Asp Pro Phe Arg Lys Asp Pro Asn Lys Leu 85 90 95 Val Leu Cys Glu Val Phe Lys Tyr Asn Arg Arg Pro Ala Glu Thr Asn 100 105 110 Leu Arg His Thr Cys Lys Arg Ile Met Asp Met Val Ser Asn Gln His 115 125Pro Trp Phe Gly Met Glu Glu Glu Tyr Thr Leu Met Gly Thr Asp Gly 130 135 140His Pro Phe Gly Trp Pro Ser Asn Gly Phe Pro Gly Pro Gln Gly Pro Tyr Tyr Cys Gly Val Gly Ala Asp Arg Ala Tyr Gly Arg Asp Ile Val Glu Ala His Tyr Arg Ala Cys Leu Tyr Ala Gly Val Lys Ile Ala Gly 180 185 Thr Asn Ala Glu Val Met Pro Ala Gln Trp Glu Phe Gln Ile Gly Pro 195 200 205 Cys Glu Gly Ile Ser Met Gly Asp His Leu Trp Val Ala Arg Phe Ile Leu His Arg Val Cys Glu Asp Phe Gly Val Ile Ala Thr Phe Asp Pro 225 230 235 Lys Pro Ile Pro Gly Asn Trp Asn Gly Ala Gly Cys His Thr Asn Phe 245 250 255 Ser Thr Lys Ala Met Arg Glu Glu Asn Gly Leu Lys Tyr Ile Glu Glu 260 265 270 Ala Ile Glu Lys Leu Ser Lys Arg His Gln Tyr His Ile Arg Ala Tyr

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 275 280 285

Asp Pro Lys Gly Gly Leu Asp Asn Ala Arg Arg Leu Thr Gly Phe His Glu Thr Ser Asn Ile Asn Asp Phe Ser Ala Gly Val Ala Asn Arg Ser 305 310 315 Ala Ser Ile Arg Ile Pro Arg Thr Val Gly Gln Glu Lys Lys Gly Tyr 325 330 335Phe Glu Asp Arg Arg Pro Ser Ala Asn Cys Asp Pro Phe Ser Val Thr 340 345Glu Ala Leu Ile Arg Thr Cys Leu Leu Asn Glu Thr Gly Asp Glu Pro 355 360 365 Phe Gln Tyr Lys Asn

<210> 193 <211> 379 <212> PRT <213> Homo sapiens

WO 2004/009622

Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu Asp Leu Phe 1 10 15

Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly Thr Arg Gly 35 40 45

Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn Thr Val Glu 50 60

Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile Asn Lys Arg 65 70 75 80

Gly Ala Ser Tyr Ile Leu Lys Leu Ala Asn Arg Leu Tyr Gly Glu Lys 85 90 95

Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln Lys Thr Tyr

Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser Glu Asp Ala 115 120 125

Arg Lys Thr Ile Asn Gln Trp Val Lys Gly Gln Thr Glu Gly Lys Ile 130 135 140

Pro Glu Leu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val 145 150 160

Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met
165 170 175

Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg 180 185 190

Lys Thr Val Lys Met Met Tyr Gln Lys Lys Lys Phe Ala Tyr Gly Tyr
195 200 205

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Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu 210 215 220

Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser 225 230 235 240 Thr Gly Leu Lys Lys Ile Glu Glu Glu Leu Thr Leu Glu Lys Leu His 245 250 255 Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn Val Ser Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu 275 280 285 Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu 290 295 300 Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala 325 Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn Phe 340 350 Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser Gly 365 365 Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro

<210> 194 <211> 271 <212> PRT <213> Homo sapiens

Met Ala Ala Pro Gln Asp Val His Val Arg Ile Cys Asn Gln Glu Ile 1 10 15

Cys Ser Gly Pro Leu Ser Ala Leu Thr Glu Leu Asn Thr Lys Val Lys 35 40 45

Glu Lys Phe Gln Gln Leu Arg His Arg Ile Gln Pro Val Leu Tyr Gln
50 60

Arg Ala Phe Ile Trp Thr Ala Ser Thr Phe Phe Phe Lys Leu Thr Tyr

Ser Leu Thr Asp Phe Ser Ser Thr Gln His Asp Phe Asn Ser Pro Thr 85 90 95

Thr Pro Val Thr Phe Ser Asp Leu Glu Gln Leu Ala Lys Glu Gln Asp $100 \hspace{1cm} 105 \hspace{1cm} 110$

Lys Glu Ser Glu Lys Gln Leu Leu Leu Gln Glu Val Glu Asn His Lys

Lys Gln Met Leu Ser Asn Gln Ala Ser Trp Arg Lys Ala Asn Leu Thr 130 135 140



protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Cys Lys Ile Ala Ile Asp Asm Leu Glu Lys Ala Glu Leu Leu Glm Gly

Gly Asp Leu Leu Arg Gln Arg Lys Thr Thr Lys Glu Ser Leu Ala Gln 165 170 175 Thr Ser Ser Thr Ile Thr Glu Ser Leu Met Gly Ile Ser Arg Met Met
180 185 190 Ala Gln Gln Val Gln Gln Ser Glu Glu Ala Met Gln Ser Leu Val Thr 195 200 205 Ser Ser Arg Thr Ile Leu Asp Ala Asn Glu Glu Phe Lys Ser Met Ser Gly Thr Ile Gln Leu Gly Arg Lys Leu Ile Thr Lys Tyr Asn Arg Arg 225 230 235 Glu Leu Thr Asp Lys Leu Leu Ile Phe Leu Ala Leu Arg Leu Phe Leu 250 255 Ala Thr Val Leu Tyr Ile Val Lys Lys Arg Leu Phe Pro Phe Leu 260 265 270

<210> 195 <211> 314 <212> PRT <213> Homo sapiens

Met Glu Gly Val Glu Leu Lys Glu Glu Trp Gln Asp Glu Asp Phe Pro 1 10 15

Ile Pro Leu Pro Glu Asp Asp Ser Ile Glu Ala Asp Ile Leu Ala Ile 20 25 30

Thr Gly Pro Glu Asp Gln Pro Gly Ser Leu Glu Val Asn Gly Asn Lys 35 40 45

Val Arg Lys Leu Met Ala Pro Asp Ile Ser Leu Thr Leu Asp Pro

Ser Asp Gly Ser Val Leu Ser Asp Asp Leu Asp Glu Ser Gly Glu Ile

Asp Leu Asp Gly Leu Asp Thr Pro Ser Glu Asn Ser Asn Glu Phe Glu 85 90 95

Trp Glu Asp Asp Leu Pro Lys Pro Lys Thr Thr Glu Val Ile Arg Lys

Gly Ser Ile Thr Glu Tyr Thr Ala Ala Glu Glu Lys Glu Asp Gly Arg 115 120 125

Arg Trp Arg Met Phe Arg Ile Gly Glu Gln Asp His Arg Val Asp Met

Lys Ala Ile Glu Pro Tyr Lys Lys Val Ile Ser His Gly Gly Tyr Tyr 145 150 155 160

Gly Asp Gly Leu Asn Ala Ile Val Val Phe Ala Val Cys Phe Met Pro 165 170 175

Glu Ser Ser Gln Pro Asn Tyr Arg Tyr Leu Met Asp Asn Leu Phe Lys



Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Tyr Val Ile Gly Thr Leu Glu Leu Leu Val Ala Glu Asn Tyr Met Ile Val Tyr Leu Asn Gly Ala Thr Thr Arg Arg Lys Met Pro Ser Leu Gly 210 220 Trp Leu Arg Lys Cys Tyr Gln Gln Ile Asp Arg Arg Leu Arg Lys Asn 225 230 235 Leu Lys Ser Leu Ile Ile Val His Pro Ser Trp Phe Ile Arg Thr Leu 245 250 255 Leu Ala Val Thr Arg Pro Phe Ile Ser Ser Lys Phe Ser Gln Lys Ile 260 265 . Arg Tyr Val Phe Asn Leu Ala Glu Leu Ala Glu Leu Val Pro Met Glu 275 280 285 Tyr Val Gly Ile Pro Glu Cys Ile Lys Gln Val Asp Gln Glu Leu Asn 290 300

196 193 PRT

Homo sapiens

Gly Lys Gln Asp Glu Pro Lys Asn Glu Gln 305

WO 2004/009622

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Glu Glu Glu Gln Trp Ala Arg Glu Ile Gly Ala Gln Leu Arg Arg Met

Gln Arg His Arg Pro Ser Pro Trp Arg Val Leu Tyr Asn Leu Ile Met

Gly Leu Leu Pro Leu Pro Arg Gly His Arg Ala Pro Glu Met Glu Pro





Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 180 185

<210> <211> <212> <213> 197 648

Homo sapiens

<400> 197

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Phe Lys Asp Ala Val Phe Asp Gly Ser Ser Cys Ile Ser Pro Thr Ile $20 \hspace{1cm} 25 \hspace{1cm} 30$

Val Gln Gln Phe Gly Tyr Gln Arg Arg Ala Ser Asp Asp Gly Lys Leu

Thr Asp Pro Ser Lys Thr Ser Asn Thr Ile Arg Val Phe Leu Pro Asn 50 60

Lys Gln Arg Thr Val Val Asn Val Arg Asn Gly Met Ser Leu His Asp 65 70 75 80

Cys Leu Met Lys Ala Leu Lys Val Arg Gly Leu Gln Pro Glu Cys Cys 85 90 95

Ala Val Phe Arg Leu Leu His Glu His Lys Gly Lys Lys Ala Arg Leu 100 105 110

Asp Trp Asn Thr Asp Ala Ala Ser Leu Ile Gly Glu Glu Leu Gln Val

Asp Phe Leu Asp His Val Pro Leu Thr Thr His Asn Phe Ala Arg Lys 130 140

Thr Phe Leu Lys Leu Ala Phe Cys Asp Ile Cys Gln Lys Phe Leu Leu 145 150 155 160

Asn Gly Phe Arg Cys Gln Thr Cys Gly Tyr Lys Phe His Glu His Cys 165 170 175

Ser Thr Lys Val Pro Thr Met Cys Val Asp Trp Ser Asn Ile Arg Gln 180 185 190

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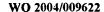
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Asn Thr Ser Ser Pro Ser Ser Glu Gly Ser Leu Ser Gln Arg Gln Arg 245 250 255

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Asp Ser Arg Met Ile Glu Asp Ala Ile Arg Ser His Ser Glu Ser Ala 275 280 285





Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Ser Pro Ser Ala Leu Ser Ser Pro Asn Asn Leu Ser Pro Thr Gly 290 295 300

Trp Ser Gln Pro Lys Thr Pro Val Pro Ala Gln Arg Glu Arg Ala Pro 305 310 320 Val Ser Gly Thr Gln Glu Lys Asn Lys Ile Arg Pro Arg Gly Gln Arg 325 335 Asp Ser Ser Tyr Tyr Trp Glu Ile Glu Ala Ser Glu Val Met Leu Ser Thr Arg Ile Gly Ser Gly Ser Phe Gly Thr Val Tyr Lys Gly Lys Trp 355 360 365 His Gly Asp Val Ala Val Lys Ile Leu Lys Val Val Asp Pro Thr Pro 370 380 Glu Gln Phe Gln Ala Phe Arg Asn Glu Val Ala Val Leu Arg Lys Thr 385 390 395 400 Arg His Val Asn Ile Leu Leu Phe Met Gly Tyr Met Thr Lys Asp Asn 405 410 415 Leu Ala Ile Val Thr Gln Trp Cys Glu Gly Ser Ser Leu Tyr Lys His 420 425 430 Leu His Val Gln Glu Thr Lys Phe Gln Met Phe Gln Leu Ile Asp Ile 435 440 445 Ala Arg Gln Thr Ala Gln Gly Met Asp Tyr Leu His Ala Lys Asn Ile 450 455 460 Ile His Arg Asp Met Lys Ser Asn Asn Ile Phe Leu His Glu Gly Leu 465 470 475 480 Thr Val Lys Ile Gly Asp Phe Gly Leu Ala Thr Val Lys Ser Arg Trp 485 490 495 Ser Gly Ser Gln Gln Val Glu Gln Pro Thr Gly Ser Val Leu Trp Met 500 505 510 Ala Pro Glu Val Ile Arg Met Gln Asp Asn Asn Pro Phe Ser Phe Gln 515 520 525 Ser Asp Val Tyr Ser Tyr Gly Ile Val Leu Tyr Glu Leu Met Thr Gly 530 540 Glu Leu Pro Tyr Ser His Ile Asn Asn Arg Asp Gln Ile Ile Phe Met 545 550 560 Val Gly Arg Gly Tyr Ala Ser Pro Asp Leu Ser Lys Leu Tyr Lys Asn 565 570 575 Cys Pro Lys Ala Met Lys Arg Leu Val Ala Asp Cys Val Lys Lys Val Lys Glu Glu Arg Pro Leu Phe Pro Gln Ile Leu Ser Ser Ile Glu Leu S95 600 605 Leu Gln His Ser Leu Pro Lys Ile Asn Arg Ser Ala Ser Glu Pro Ser Leu His Arg Ala Ala His Thr Glu Asp Ile Asn Ala Cys Thr Leu Thr



PCT/EP2003/007835

Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt Thr Ser Pro Arg Leu Pro Val Phe 645

198 399

PRT Homo sapiens <400> 198 Met Tyr Ser Pro Arg Gly Ser Gln Gly Arg Gly Thr Ala Glu Ala Thr Ala Asn Ser Pro Ser Pro Pro Ile Ala Pro Ser His Ser Arg Val Thr Phe Ser Leu Ser Thr Leu His Thr Leu Ser Pro Pro Pro Arg Pro Phe 35 40 45 Pro Ser Val Ser Arg Ala Ala Ala Gln Lys Pro His His Leu His Pro His Ile Leu Leu Ala Gly Ser Ala Ala Val Pro Pro Arg Val Leu Lys 65 70 75 80 Ala Glu Met Asn Asn Thr Ala Ala Ser Pro Met Ser Thr Ala Thr Ser Ser Ser Gly Arg Ser Thr Gly Lys Ser Ile Ser Phe Ala Thr Glu Leu 100 105 110 Gln Ser Met Met Tyr Ser Leu Gly Asp Ala Arg Arg Pro Leu His Glu 115 120 125 Thr Ala Val Leu Val Glu Asp Val Val His Thr Gln Leu Ile Asn Leu 130 135 140 Leu Gln Gln Ala Ala Glu Val Ser Gln Leu Arg Gly Ala Arg Val Ile 145 150 160 Thr Pro Glu Asp Leu Leu Phe Leu Met Arg Lys Asp Lys Lys Leu
165 170 175 Arg Arg Leu Leu Lys Tyr Met Phe Ile Arg Asp Tyr Lys Ser Lys Ile 180 185 190 Val Lys Gly Ile Asp Glu Asp Asp Leu Leu Glu Asp Lys Leu Ser Gly 195 200 205 Ser Asn Asn Ala Asn Lys Arg Gln Lys Ile Ala Gln Asp Phe Leu Asn 210 225 220 Ser Ile Asp Gln Thr Gly Glu Leu Leu Ala Met Phe Glu Asp Asp Glu 225 230 235 240 Ile Asp Glu Val Lys Gln Glu Arg Met Glu Arg Ala Glu Arg Gln Thr 245 250 255 Arg Ile Met Asp Ser Ala Gln Tyr Ala Glu Phe Cys Glu Ser Arg Gln 260 265 270 Leu Ser Phe Ser Lys Lys Ala Ser Lys Phe Arg Asp Trp Leu Asp Cys 285 Ser Ser Met Glu Ile Lys Pro Asn val Val Ala Met Glu Ile Leu Ala







Protein Complexes of cellular networks underlying the development of cancer and other diseases.ST25.txt 290 295 300

Tyr Leu Ala Tyr Glu Thr Val Ala Gln Leu Val Asp Leu Ala Leu Leu 320

Val Arg Gln Asp Met Val Thr Lys Ala Gly Asp Pro Phe Ser His Ala 335

Ile Ser Ala Thr Phe Ile Gln Tyr His Asn Ser Ala Glu Ser Thr Ala 340

Ala Cys Gly Val Glu Ala His Ser Asp Ala Ile Gln Pro Cys His Ile 355

Arg Glu Ala Ile Arg Arg Tyr Ser His Arg Ile Gly Pro Leu Ser Pro Phe Thr Asn Ala Tyr Arg Arg Arg Asn Gly Met Ala Phe Leu Ala Cys 385